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A Retrospective Cross-Sectional Study on Antimicrobial Usage and Resistance Rate of Microorganisms in Bintulu Hospital

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ABSTRACT

Introduction: Treatment of infectious diseases with antimicrobials had greatly reduced premature deaths from infections. However, the overuse of antimicrobials have contributed to the emergence of antimicrobial resistance. Evaluation of local antimicrobial usage patterns and resistance rate of microorganisms are beneficial to promote judicious use of antimicrobial therapy. This study aimed to determine the usage pattern of antimicrobials and its correlation with resistance rate of the most commonly isolated microorganisms in Bintulu Hospital.

Methods: This study was a retrospective cross-sectional study on the antimicrobial usage of 17 injectable antimicrobials under the Malaysian National Surveillance of Antibiotic Utilisation and its correlation with the resistance rates of microorganisms in adult wards of Bintulu Hospital between 1st January 2018 and 31st December 2019.

Results: An increase of 19.7% in the overall antimicrobial usage was observed in 2019 as compared to 2018. β-lactam/β-lactamase inhibitors and cephalosporins were the most prescribed antimicrobial groups in Bintulu Hospital during the study period. The two groups have contributed to 96.0% of total antimicrobial usage. *Klebsiella pneumoniae, Escherichia coli* and *Pseudomonas*

aeruginosa were the most common microorganisms isolated from all types of samples collected from the wards.

Conclusion: Significant differences were observed between antimicrobial usage and resistance rate of commonly isolated microorganisms between 2018 and 2019. Significant correlations between the usage and resistance rate were also observed. Therefore, stricter monitoring, active prospective audits and antimicrobial stewardship are essential to minimise the risk of antimicrobial resistance.

Keywords: Antimicrobial resistance, antimicrobial stewardship, defined daily dose

INTRODUCTION

Infection is the most common cause of hospital visits and the use of antimicrobial agents had greatly reduced the incidence of premature death (1). However, the overuse of antimicrobial agents for dubious indications and the prolonged treatment period have contributed to the emergence of antimicrobial resistance. Studies have shown that up to 50.0% of all antimicrobials prescribed are considered unnecessary (2,3). A 200.0% increase in antimicrobial consumption has been estimated in 2030 assuming that there is no policy change in the immediate future (4).

There are 18 antibiotics monitored under the Malaysian National Surveillance on Antibiotic Utilisation. In Malaysia, an increment of 7.3% in total antibiotic utilisation had been observed in 2018 as compared to 2017. In intensive care units (ICU), the utilisation of antimicrobial has increased by 0.47%. Four antibiotic groups that had increased utilisations in all wards and ICU include penicillin/β-lactamase inhibitor combination, glycopeptides, fluoroquinolones, and cephalosporins (5). The National Surveillance of Antimicrobial Resistance Malaysia also reported an increased resistance rate of several microorganisms, including *Streptococcus pneumoniae, Escherichia coli,* and *Klebsiella pneumoniae* (6).

Bronzwaer et al. found a correlation between antimicrobial resistance and antimicrobial use (7). The concentration of antimicrobial prescriptions is at its highest in inpatient settings in European hospitals with 30.0-40.0% of the patients on antibiotics (8,9). With increased antimicrobial resistance, healthcare providers are left with a limited choice of antimicrobial agents, which poses a major threat to public health (1).

Therefore, national surveillance of antibiotic usage are essential in order to monitor national usage trend, which provides the baseline data for future epidemiological analysis of the association between antimicrobial consumption and resistance rates (10). World Health Organisation (WHO) has assigned the Anatomical Therapeutic Chemical/Defined daily dose (ATC/DDD) system as a tool for drug utilisation monitoring and research. DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults (11). Thus, the use of DDD enable researchers to analyse drug consumptions between populations and its usage trends.

The evaluation on usage patterns of antimicrobial agents and resistance rate of microorganisms in the local setting is beneficial in promoting judicious use of antimicrobials. This study aimed to explore the usage pattern of antimicrobial agents and its correlation with resistance rate of the most commonly isolated microorganisms in Bintulu Hospital.

METHODS

Study Design

This study was a retrospective, cross-sectional study on the antimicrobial usage of 17 injectable antimicrobials under the Malaysian National Surveillance of Antibiotic Utilisation and resistance rate of microorganisms in adult wards of Bintulu Hospital between 1st January 2018 and 31st December 2019. The antibiotics included were penicillin/β-lactamase inhibitor, cephalosporins, fluoroquinolones, carbapenems, polymyxins and aminoglycoside. The usage of oral antibiotics, prescriptions involving paediatric patients, penicillins (ampicillin injection, benzylpenicillin injection, cloxacillin injection), aminoglycosides (streptomycin injection), macrolides (erythromycin lactobionate injection, azithromycin injection). Other antibiotics including metronidazole injection, clindamycin injection were excluded from this study. The study was approved by the Medical Research & Ethics Committee, Malaysia (NMRR-20-60-52689).

Data Collection

The antimicrobial usage was acquired based on the number of vials of the agents issued to the wards by retrieving the pharmacy issuance record. The antimicrobial injections usage were reported quarterly in March, June, September and December of each year. Data on patient days was obtained from hospital administration office in order to calculate DDD for each antibiotic by using the following formula:

$$\frac{DDD}{year} = \frac{T}{DDD}$$

T= total amount of antibiotic used per year

DDD = DDD assigned for antibiotic based on the ATC/DDD system

$$\frac{DDD}{1000\ patient\ days} = \frac{DDD\ per\ year}{P} \times 1000$$

P= total patient days

Subsequently, we compared the antimicrobial usage between 2018 and 2019. In our study, resistance rate was obtained from the laboratory in Bintulu Hospital. The three most commonly isolated microorganisms were identified and the resistance rates were compared between 2018 and 2019. The resistance rate of microorganisms were reported quarterly.

Statistical Analysis

The data analysis was conducted by using the Statistical Package for the Social Sciences (SPSS) version 21. Antimicrobial usage and resistance rates of microorganisms across the wards were summarised using descriptive statistics. Mann-Whitney test was used to compare the antimicrobial usage and resistance rate. The correlation between antimicrobial usage and resistance rate of the most commonly isolated microorganisms were evaluated using Spearman correlation. A *P*-value of <0.05 was considered to be statistically significant.

RESULTS

Table 1 shows the change in the antimicrobial usage between 2018 and 2019. A significant increase in the usage of ampicillin/sulbactam, amoxicillin/clavulanate, cefoperazone and meropenem (*P*=0.02) was observed.

Table 1: Comparison on the usage of selected injectable antimicrobials in Bintulu Hospital between 2018 and 2019

Antimicrobials	Median (IQR)		Z statistic[a]	*P*-value[a]
	Year 2018	Year 2019		
Ampicillin/sulbactam	10.70 (5.18)[b]	17.73 (4.28)[c]	-2.31	**0.02**
Amoxicillin/clavulanate	67.91 (7.37)[b]	88.53 (22.84)[b]	-2.31	**0.02**
Piperacillin/tazobactam	22.76 (6.35)[b]	30.23 (8.45)[c]	-1.73	0.08
Cefuroxime	38.08 (9.66)[b]	40.83 (2.50)[b]	-0.87	0.39
Ceftriaxone	60.09 (14.30)[c]	46.77 (24.03)[b]	-0.58	0.56
Cefotaxime	1.14 (1.20)[b]	0.52 (0.94)[b]	-1.44	0.15
Ceftazidime	47.83 (24.64)[b]	68.45 (18.27)[c]	-1.73	0.08
Cefoperazone	10.02 (5.80)[b]	17.16 (4.20)[b]	-2.31	**0.02**
Cefoperazone/sulbactam	0.00 (0.00)	0.00 (0.00)	0.00	>0.95
Cefepime	6.03 (3.17)[c]	3.63 (4.12)[b]	-0.58	0.56
Ciprofloxacin	0.05 (0.68)[b]	0.31 (0.61)[b]	-0.58	0.56
Ertapenem	1.50 (0.99)[c]	1.42 (1.10)[c]	-0.15	0.89
Meropenem	3.82 (2.76)[b]	2.57 (2.34)[c]	-2.31	**0.02**

Table 1: *Continued*

Antimicrobials	Median (IQR)		Z statistic[a]	*P*-value[a]
	Year 2018	Year 2019		
Imipenem/cilastatin	0.06 (0.41)[b]	0.58 (0.36)[c]	-1.75	0.08
Polymyxin E	0.00 (0.00)	0.00 (0.00)	0.00	>0.95
Gentamicin	3.22 (0.92)[c]	3.00 (4.30)[b]	-0.15	0.89
Amikacin	0.16 (0.41)[b]	0.39 (1.29)[b]	-1.16	0.25

[a] Mann- Whitney test
[b] Skew to the right
[c] Skew to the left

In this study, we reported *Klebsiella pneumoniae*, *Escherichia coli* and *Pseudomonas aeruginosa* as the most common microorganisms isolated from all types of samples collected from adult wards in Bintulu Hospital (Table 2). Thus, vancomycin was excluded from the data analysis as methicillin-resistant *Staphylococcus aureus* was not commonly isolated.

Table 2: Comparison on the resistance rates of the three most common microorganisms isolated in Bintulu hospital between 2018 and 2019

Antimicrobials	Median (IQR)		Z statistic[a]	*P*-value[a]
	Year 2018	Year 2019		
Ampicillin/sulbactam				
Klebsilla pneumonia	24.60 (8.42)[c]	19.45 (3.52)[c]	-1.74	0.08
Escherichia coli	25.05 (17.05)[c]	12.05 (4.55)[b]	-2.02	0.04
Pseudomonas aeruginosa	0.00 (0.00)	0.00 (0.00)	0.00	> 0.95
Amoxicillin/clavulanate				
Klebsilla pneumonia	14.10 (3.08)[b]	12.65 (6.98)[b]	-0.58	0.56
Escherichia coli	13.65 (8.25)[b]	12.45 (5.68)[c]	-1.14	0.25
Pseudomonas aeruginosa	0.00 (0.00)	0.00 (0.00)	0.00	> 0.95
Piperacillin/tazobactam				
Klebsilla pneumonia	3.10 (1.20)[c]	5.05 (5.28)[b]	-1.60	0.11
Escherichia coli	1.10 (3.18)[b]	0.75 (1.50)	-0.62	0.54
Pseudomonas aeruginosa	1.95 (2.98)[c]	0.70 (0.88)[c]	-1.17	0.24
Cefuroxime				
Klebsilla pneumonia	17.20 (9.65)[b]	18.70 (1.45)[b]	0.00	1.00
Escherichia coli	16.45 (3.20)[b]	18.15 (9.08)[c]	-0.58	0.56
Pseudomonas aeruginosa	0.00 (0.00)	0.00 (0.00)	0.00	> 0.95

Table 2: *Continued*

Antimicrobials	Median (IQR)		Z statistic[a]	*P*-value[a]
	Year 2018	Year 2019		
Ceftriaxone				
Klebsilla pneumonia	0.00 (0.00)	1.25 (1.55)[c]	-1.98	0.05
Escherichia coli	0.00 (0.00)	0.00 (0.00)	0.00	> 0.95
Pseudomonas aeruginosa	0.00 (0.00)	0.00 (0.00)	0.00	> 0.95
Cefotaxime				
Klebsilla pneumonia	17.00 (9.05)[b]	21.70 (4.55)[b]	-1.16	0.25
Escherichia coli	13.40 (10.75)[c]	19.50 (20.60)[b]	-1.44	0.15
Pseudomonas aeruginosa	0.00 (0.00)	0.00 (0.00)	0.00	> 0.95
Ceftazidime				
Klebsilla pneumonia	12.00 (6.57)[b]	16.25 (2.45)[b]	-1.44	0.15
Escherichia coli	5.00 (9.53)[b]	6.65 (7.42)[b]	-0.29	0.77
Pseudomonas aeruginosa	3.20 (2.68)[c]	2.90 (4.43)[c]	-0.58	0.56
Cefoperazone				
Klebsilla pneumonia	17.15 (9.15)[b]	21.70 (3.72)[b]	-1.44	0.15
Escherichia coli	14.70 (3.75)[b]	19.40 (19.27)[b]	-1.16	0.25
Pseudomonas aeruginosa	7.00 (5.05)[c]	4.80 (3.00)[c]	-1.44	0.15
Cefoperazone/sulbactam				
Klebsilla pneumonia	0.00 (0.00)	0.00 (0.00)	0.00	>0.95
Escherichia coli	0.00 (0.00)	0.00 (0.00)	0.00	> 0.95
Pseudomonas aeruginosa	0.00 (0.00)	0.00 (0.00)	0.00	> 0.95
Cefepime				
Klebsilla pneumonia	11.05 (6.13)[c]	15.9 (2.47)[c]	-2.02	0.04
Escherichia coli	3.90 (3.50)[b]	8.85 (17.05)[b]	-1.16	0.25
Pseudomonas aeruginosa	1.60 (3.73)[b]	1.45 (2.70)[b]	-0.15	0.89
Ciprofloxacin				
Klebsilla pneumonia	5.60 (8.60)[b]	6.65 (3.22)[b]	-0.29	0.77
Escherichia coli	18.45 (4.95)[c]	15.10 (7.10)[c]	-0.87	0.39
Pseudomonas aeruginosa	1.85 (1.75)[c]	1.35 (5.65)[b]	-0.29	0.77
Ertapenem				
Klebsilla pneumonia	2.20 (2.08)[c]	0.25 (0.57)[b]	-2.32	0.03
Escherichia coli	0.60 (2.40)[b]	0.00 (1.13)[b]	-0.66	0.51
Pseudomonas aeruginosa	0.00 (0.00)	0.00 (0.00)	0.00	> 0.95
Meropenem				
Klebsilla pneumonia	0.00 (1.73)[b]	0.00 (0.00)	-1.00	0.32
Escherichia coli	0.00 (0.00)	0.00 (1.13)[b]	-1.00	0.32
Pseudomonas aeruginosa	1.90 (6.82)[b]	3.20 (4.63)[b]	0.00	> 0.95

Table 2: *Continued*

Antimicrobials	Median (IQR)		Z statistic[a]	*P*-value[a]
	Year 2018	Year 2019		
Imipenem/cilastatin				
Klebsilla pneumonia	0.00 (0.00)	0.00 (0.00)	0.00	> 0.95
Escherichia coli	0.00 (0.00)	0.00 (1.13)[b]	-1.00	0.32
Pseudomonas aeruginosa	1.00 (5.90)[b]	3.70 (3.63)[b]	-0.73	0.47
Polymyxin E				
Klebsilla pneumonia	0 (0.00)	0 (0.00)	0.00	> 0.95
Escherichia coli	0 (0.00)	0 (0.00)	0.00	> 0.95
Pseudomonas aeruginosa	0 (0.00)	0 (0.00)	0.00	> 0.95
Gentamicin				
Klebsilla pneumonia	2.70 (2.78)[c]	5.60 (2.83)[b]	-2.18	0.03
Escherichia coli	19.25 (8.58)[c]	10.05 (5.13)[b]	-1.73	0.08
Pseudomonas aeruginosa	3.20 (3.15)[c]	4.95 (6.70)[c]	-0.58	0.56
Amikacin				
Klebsilla pneumonia	0.00 (0.00)	0.50 (1.53)[b]	-1.51	0.13
Escherichia coli	0.00 (1.05)[b]	0.00 (1.20)[b]	-0.19	0.85
Pseudomonas aeruginosa	1.60 (3.05)[b]	0.85 (1.40)	-0.73	0.47

[a] Mann- Whitney test

[b] Skew to the right

[c] Skew to the left

Significant increases in the resistance rate of *Klebsiella penumoniae* towards ceftriaxone (*P*=0.05), cefepime (*P*=0.04) and gentamicin (*P*=0.03) were observed. In contrast, a significant reduction in the resistance rate of *Klebsiella pneumoniae* towards ertapenem was observed (*P*=0.03). The resistance rate of *Escherichia coli* towards ampicillin/sulbactam decreased significantly (*P*=0.04). Resistance rate of *Pseudomonas aeruginosa* towards piperacillin/tazobactam, ceftazidime, cefoperazone, cefepime, ciprofloxacin, meropenem, imipenem/cilastatin, gentamicin, and amikacin (excluding antimicrobial without anti- pseudomonal activity) and no significant difference was observed.

The correlation between antimicrobial usage and resistance rate of *Klebsiella pneumoniae*, *Escherichia coli* and *Pseudomonas aeruginosa* is shown in Table 3. A positive correlation was observed between piperacillin/tazobactam and the resistance rate of *Klebsiella pneumoniae* (*P*=0.02) with a correlation coefficient (*r*) of 0.80. Meanwhile, a negative correlation was observed

between ampicillin/sulbactam and the resistance rate of *Klebsiella pneumoniae* (*P*=0.01) and *Escherichia coli* (*P*=0.02).

Table 3: Correlation between antimicrobials usage and the resistance rate of *Klebsiella pneumoniae, Escherichia coli and Pseudomonas aeruginosa*

Antimicrobials	***r***	***P*-value**
Ampicillin/sulbactam		
Klebsilla pneumonia	-0.86	0.01
Escherichia coli	-0.81	0.01
Pseudomonas aeruginosa	-	-
Amoxicillin/clavulanate		
Klebsilla pneumonia	0.11	0.79
Escherichia coli	-0.01	0.98
Pseudomonas aeruginosa	-	-
Piperacillin/tazobactam		
Klebsilla pneumonia	0.80	0.02
Escherichia coli	-0.05	0.91
Pseudomonas aeruginosa	-0.62	0.10
Cefuroxime		
Klebsilla pneumonia	-0.69	0.06
Escherichia coli	0.22	0.61
Pseudomonas aeruginosa	-	-
Ceftriaxone		
Klebsilla pneumonia	-	-
Escherichia coli	-0.57	0.14
Pseudomonas aeruginosa	-	-
Cefotaxime		
Klebsilla pneumonia	0.04	0.93
Escherichia coli	-0.57	0.15
Pseudomonas aeruginosa	-	-
Ceftazidime		
Klebsilla pneumonia	0.06	0.88
Escherichia coli	0.41	0.32
Pseudomonas aeruginosa	-0.27	0.52
Cefoperazone		
Klebsilla pneumonia	-	-
Escherichia coli	0.29	0.48
Pseudomonas aeruginosa	-0.64	0.09

Table 3: *Continued*

Antimicrobials	*r*	*P*-value
Cefoperazone/sulbactam		
Klebsilla pneumonia	-	-
Escherichia coli	-	-
Pseudomonas aeruginosa	-	-
Cefepime		
Klebsilla pneumonia	-0.49	0.22
Escherichia coli	0.48	0.22
Pseudomonas aeruginosa	0.34	0.41
Ciprofloxacin		
Klebsilla pneumonia	-0.60	0.11
Escherichia coli	0.37	0.37
Pseudomonas aeruginosa	0.42	0.35
Ertapenem		
Klebsilla pneumonia	-	-
Escherichia coli	-0.29	0.48
Pseudomonas aeruginosa	0.11	0.81
Meropenem		
Klebsilla pneumonia	0.07	0.87
Escherichia coli	-0.05	0.91
Pseudomonas aeruginosa	-0.23	0.59
Imipenem/cilastatin		
Klebsilla pneumonia	-	-
Escherichia coli	0.49	0.22
Pseudomonas aeruginosa	0.41	0.36
Polymyxin E		
Klebsilla pneumonia	-	-
Escherichia coli	-	-
Pseudomonas aeruginosa	-	-
Gentamicin		
Klebsilla pneumonia	0.32	0.44
Escherichia coli	0.15	0.73
Pseudomonas aeruginosa	0.61	0.11
Amikacin		
Klebsilla pneumonia	-0.02	0.95
Escherichia coli	0.67	0.07
Pseudomonas aeruginosa	0.29	0.49

DISCUSSION

Antimicrobial usage data is important in order to observe usage trend and its correlation with the resistance rate of microorganisms. An increase in the overall usage of antimicrobials was observed in Bintulu Hospital in 2019 as compared to 2018. β-lactam/β-lactamase inhibitors and cephalosporins groups were the most prescribed antibiotics in Bintulu Hospital which contributed to 96.0% of the total antimicrobial usage. According to Tan et al., the most commonly used antibiotics for hospitalised patients were broad-spectrum antibiotics including β-lactam/β-lactamase inhibitors and cephalosporins which comprised of 86.4% of the total antibiotic consumption (12).

High usage of ampicillin/sulbactam in 2019 was seen with DDD usage of 70.33 and an increament of 57.62% from the previous year. This was mainly attributed by the use of high dose ampicillin/sulbactam as empicical therapy and definitive treatment in multi-drug resistance *Acinetobacter baumanii*.

Our usage were generally consistent with the Malaysian Ministry of Health (MOH) hospitals, as well as the university, military, and private hospitals (5). According to the analysis on the utilisation of cephalosporin injections at Malaysian MOH, university, military, and private hospitals between 2014 and 2018, ceftriaxone usage was the highest and no increase in ceftazidime usage was observed (5). Our studies had also demonstrated that the use of ceftriaxone was the highest among the cephalosporin groups in 2018. However, in 2019, the usage of ceftazidime contributed to the highest proportion of cephalosporins use as an increase of 34.6% from 2018 was seen. The increase in ceftazidime usage in Bintulu Hospital was mainly due to its use in definitive and empirical treatment of melioidosis due to the local epidemiology

The initiation of antimicrobial stewardship program is equally important as it has managed to reduce the use of meropenem in 2019 from 2018. De-escalation therapy was introduced with prompt reviews of meropenem usage by antimicrobial stewardship pharmacists and physicians during the initiation of meropenem. This study found that meropenem was the most common carbapenem prescribed, which was also seen nationally (5). Interestingly, there was a decrease in the usage of all carbapenems (doripenem, imipenem and meropenem) except ertapenem in 2018

as compared to 2017 at the national level (5). However, such decrease was not observed in Bintulu Hospital. This may be due to the efforts of de-escalating from meropenem and imipenem to definitive therapy for extended-spectrum beta-lactamases-producing *Klebsiella penumoniae* and extended-spectrum beta-lactamases-producing *Escherichia coli.*

Klebsiella pneumoniae, *Escherichia coli* and *Pseudomonas aeruginosa* were the most common microorganisms isolated from all types of samples collected from adult wards in Bintulu Hospital. These have contributed to the high usage of β-lactam/β-lactamase inhibitors and cephalosporins groups in this study. This study has found a significant increase in the resistance rate of *Klebsiella penumoniae* towards ceftriaxone, cefepime and gentamicin. The National Surveillance of Antimicrobial Resistance Malaysia also reported an increased resistance rate of several microorganisms, including *Streptococcus pneumoniae, Escherichia coli* and *Klebsiella pneumoniae* (6). Therefore, prompt de-escalation of antimicrobials to narrower spectrum antimicrobials when culture and sensitivity results have been established is warranted in order to reduce the resistance rates. For example, the use of a combination of penicillins with narrower antimicrobial spectrum and targeted therapy will be wise once the aetiological pathogen has been identified. With prompt de-escalation, the use of third generation cephalosporins in managing conditions like severe community-acquired pneumonia and fourth generation cephalosporins (cefepime) in managing hospital-acquired pneumonia can be safe guarded.

A positive correlation was observed between the consumption of piperacillin/tazobactam and *Klebsiella pneumoniae* (P=0.02; r=0.80). The usage of piperacillin/tazobactam increased by 29.5% in 2019 as compared to 2018. Piperacillin/tazobactam is the only penicillin/β-lactamase inhibitor being monitored at national level. It is a frequently prescribed antimicrobial for hospital acquired pneumonia, necrotising fasciitis, and intra-abdominal infection in Bintulu Hospital. However, the National Antimicrobial Guideline recommended the use of amoxicillin/clavulanate in the early onset of hospital acquired pneumonia and ventilator acquired pneumonia (5). Adherence to this guideline will help to minimise unnecessary use of piperacillin/tazobactam for this indication. The use of piperacillin/tazobactam in necrotising fasciitis should be streamlined based on intra-operative culture and sensitivity. Furthermore, immediate aggressive surgical debridement is the primary treatment modality (5). Unfortunately, a prolonged duration of piperacillin/tazobactam

use had been observed despite the availability of intra-operative culture and sensitivity in Bintulu Hospital.

There was a negative correlation between the usage of ampicillin/sulbactam and resistance rates of *Escherichia coli* and *Klebsiella pneumonia*. This finding is in contrast to the study conducted by Cuisin et al. that has found otherwise (13). Ryu et al. reported positive correlation of the usage of piperacillin/tazobactam, ceftazidime and levofloxacin towards resistance rate of *Klebsiella pneumonia* (14).

This study served as surveillance data of antimicrobial usage trend and resistance pattern in major prescribing departments of a public hospital in Sarawak. The antimicrobial resistance pattern of microorganisms should serve as guidance for prescribers in choosing the best antimicrobial choice while reducing the risks of antimicrobial resistance.

The usage of all 17 types of injectables antimicrobials were retrieved manually from the pharmacy issuance record. Some data were excluded as the ward details were incomplete. The possibility of human errors are present as the recordings were done manually. Clinical indications and the appropriateness of antimicrobial choice were not studied as the study was focused solely on the antimicrobial usage. The study findings may not be generalisable to the paediatric population as they were excluded in the DDD calculation in view of the difference in dosage requirements.

All pharmacy staff should be educated to clearly indicate the ward during antimicrobial issuance. Point prevalence surveys should be incorporated during future data surveillance. Future study on the paediatric population will be beneficial to analyse the antimicrobials use and resistance rate in the population.

CONCLUSION

In conclusion, significant differences were observed between the antimicrobial usage and resistance rate of the most commonly isolated microorganisms. β-lactam/β-lactamase inhibitors and cephalosporins groups were the most commonly prescribed antimicrobials. *Klebsiella pneumoniae*, *Escherichia coli* and *Pseudomonas aeruginosa* were the most commonly isolated

microorganisms in Bintulu Hospital over the study period. Significant correlations were observed between antimicrobial usage and resistance rate. Stricter monitoring, active prospective audits and antimicrobial stewardship are essential to minimise the risk antimicrobial resistance.

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REFERENCES

1. Ministry of Health Malaysia. Protocol on Antimicrobial Stewardship Program in Healthcare Facilities. Pharmaceutical Services Division, Medical Development Division and Family Health Development Division. 2014.
2. Holmes AH, Moore LS, Sundsfjord A, Steinbakk M, Regmi S, Karkey A, et al. Understanding the Mechanisms and Drivers of Antimicrobial Resistance. Lancet. 2016;387(10014):176-187.
3. Dadgostar O. Antimicrobial Resistance: Implications and Costs. Infect Drug Resist. 2019;12:3903-3910.
4. Kwa A, Tan TY, Lye D, Ling ML. Reducing Antimicrobial Resistance through Appropriate Antibiotic Usage in Singapore. Singapore Medical Journal. 2008;49(10):749.
5. Ministry of Health Malaysia. National Antibiotic Guidelines 2019. Pharmaceutical Services Programmes. 2019.
6. Ministry of Health Malaysia. National Antibiotic Resistance Surveillance Report 2017. [Internet] 2017 [cited 2020 January 13] Available from: https://www.imr.gov.my/images/uploads/NSAR/NSAR_2017/NSAR_report_2017-edited- 31.1.2019
7. Bronzwaer SL, Cars O, Buchholz U, Molstad S, Goettsch W, Veldhuijzen IK, et al. The Relationship between Antimicrobial Use and Antimicrobial Resistance in Europe. Emerging Infectious Diseases. 2002;8(3):278-82.
8. Klein EY, Van Boeckell TP, Martinez RM, Pant S, Gandra S, Levin S, et al. Global Increases and Geographic Convergence in Antibiotic Consumption Between 2000 and 2015. Proc Natl Acad Sci USA. 2018;115(15):E3463-E3470.

9. Aslam B, Wang W, Arshard MI, Khursid M, Muzammil S, Rasool MH, et al. Antibiotic Resistance: A Rundown of a Global Crisis. Infect Drug Resist. 2018;11:1645-1658.
10. Marston HD, Dixon DM, Knisely JM, Palmore TN, Fauci AS. Antimicrobial Resistance. JAMA. 2016;316(11):1193-1204.
11. World Health Organisation. Purpose of the ATC/DDD system. [Internet] 2018 [cited 2020 January 13] Available from: https://www.whocc.no/atc_ddd_methodology/purpose_of_the_atc_ddd_system/
12. Tan SY, Khan RA, Khalid KE, Chong CW, Bakhtiar A. Correlation Between Antibiotic Consumption and the Occurrence of Multidrug- Resistant Organisms in a Malaysian Tertiary Hospital: A 3- Year Oservational Study. Nature Porfolio. 2022;12(3106):5-7.
13. Cuisini A, Herren D, Butikofer L, Pluss-Suard C, Kronenberg A, Marschall J. Intra-Hospital Differences in Antibiotic Use Correlate with Antimicrobial Resistance Rate in *Escherichia coli* and *Klebsiella pneumoniae*: A Retrospective Observational Study. Antimicrob Resist Infect Control. 2018;7(89):1-11.
14. Ryu S, Klein E, Chun B. Temporal Association between Antibiotic Use and Resistance in *Klebsiella pneumoniae* at a Tertiary Care Hospital. Antimicrob Resist Infect Control. 2018;7(83):1-6.