

REVIEW ARTICLE

Impact of COVID-19 towards antibiotic consumption in a major specialist hospital: A non-COVID-19 hospital perspective

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ABSTRACT

The Coronavirus disease 2019 (COVID-19) pandemic heavily affected healthcare services and medication supply. Literatures showed that the consumption of antibiotics was significantly increased during the pandemic especially in COVID-19 hospitals, however, little is known about the collateral impact of the pandemic in non-COVID-19 healthcare settings, such as Hospital Queen Elizabeth II (HQEII) based in Malaysia. This study aimed to compare the prevalence of antibiotic consumption before (2018 & 2019) and during (2020 & 2021) the pandemic, and to explore its impact on antibiotic-acquired cost and bacterial resistance. This is a descriptive observational study where the antibiotic consumption from 1st January 2018 to 31st December 2021 in HQEII was reviewed. The antibiotics selected were Meropenem, Vancomycin, Piperacillin-tazobactam, Ceftazidime and Ceftriaxone. The antibiotic consumption, antibiotic-acquired cost and cases of multidrug resistant organism (MRO) before (2018 & 2019) and during (2020 & 2021) the COVID-19 pandemic were compared, with combined 2 years data for comparison. The overall consumption of the selected antibiotics significantly increased by 45.2% (34.8 vs 50.5, $p < 0.001$) during the COVID-19 pandemic. Intensive care unit had the highest increase in antibiotic consumption (+114.3%, $p < 0.001$). There was a raising trend for the use of Vancomycin, Meropenem, Ceftazidime and Piperacillin-Tazobactam ($p < 0.005$). All

these contributed to a significant increase in antibiotic-acquired cost by 64.4% during the COVID-19 pandemic (RM909,898.80 vs RM1,486,791.20, $p < 0.001$). Notably, cases of multidrug resistant organisms also increased, especially MRO *Acinetobacter* (+197%) and Carbapenem-resistant Enterobacterales (+92%). High antibiotic consumption, antibiotic-acquired cost and MRO cases were observed in non-COVID-19 healthcare setting during the pandemic, but the factors contributing to the surge were not explored in this study.

INTRODUCTION

The Coronavirus disease 2019 (COVID-19) pandemic had led to national quarantine and movement restrictions in Malaysia on 18th March 2020. Local hospitals faced challenges to care for the exponentially growing number of infected patients while running short of ventilators and medical equipment. Most non-COVID-19 healthcare services were interrupted, reducing patients' accessibility to receive usual treatment and monitoring (Assefa et al., 2021). The surge in COVID-19 patients and other critically ill patients also led to shortage of medication supplies due to higher demand during the pandemic (Shuman et al., 2020).

Previous literatures showed that there was a significant upshift in the antibiotic usage during the COVID-19 pandemic, especially Cephalosporins (Hussein et al., 2022; Nandi et al., 2023). Although secondary bacterial infection in COVID-19 patients was relatively uncommon, empirical antibiotic treatment was still often prescribed (Granata et al., 2022). In such cases, guidelines warned that the overuse of antibiotic increases the risk of antimicrobial resistance (Living Guidance for Clinical Management of COVID-19: Living Guidance, 2021). While most studies were done in COVID-19 isolation hospitals, only few revealed the collateral impact of the pandemic towards antibiotic consumption in non-

COVID-19 healthcare settings (da Silva et al., 2021).

Hospital Queen Elizabeth II (HQEII) is a non-COVID-19 hospital based in Sabah, Malaysia. This study aims to investigate and compare the consumption of Vancomycin, Meropenem, Ceftazidime and Piperacillin-Tazobactam in HQEII before and during COVID-19 pandemic. This study also explores the antibiotic-acquired cost and bacterial resistance pattern as a result of changes in antibiotic consumption, if any. The results of this study would be useful in implying whether there is a need to monitor and further promote the optimisation of antibiotic use.

METHODS

This is a descriptive observational study where the antibiotic consumption from 1st January 2018 to 31st December 2021 in HQEII was reviewed. The selected antibiotics were Meropenem, Vancomycin, Piperacillin-tazobactam, Ceftazidime and Ceftriaxone. These antibiotics were selected because their consumption exceeded the upper limit of the national antimicrobial usage in 2020. In our setting, all antibiotics that are prescribed to patients will be transcribed into pharmacy supply database. The number of vials of antibiotics was identified through pharmacy supply database. The antibiotic consumption was then converted into defined daily dose (DDD) by dividing the number of grams supplied with the 2019-2020 ATC/DDD index assigned by the World Health Organisation (WHO) (WHOC - ATC/DDD Index, n.d.). For combination antibiotics, the assigned DDD is based on the main principal drug rather than the whole combination product. For example, the DDD for piperacillin-tazobactam will only take into account the grams of piperacillin as the main principal drug. The DDD was presented as the DDD per 1000 patient days. Table 1 shows the antibiotics selected for this study and their corresponding DDDs.

Table 1: Antibiotics WHO ATC/DDD index 2020

Antibiotic	WHO assigned DDD index
Meropenem	3
Vancomycin	2
Piperacillin-tazobactam	14
Ceftazidime	4
Ceftriaxone	2

The antibiotic-acquired cost was calculated by multiplying the number of vials of the antibiotics to the cost of each vial, at the time of purchase.

organisms. Specifically, DDD was used to compare for the antibiotic consumption. The independent T-test was used to compare the antibiotic consumption and cost before (2018 & 2019) and during (2020 & 2021) the COVID-19 pandemic as the data was normally distributed.

Ethics Statement

This study was approved by the Medical Research and Ethics Committee with the identification code NMRR ID-22-00863-AET, which complies with the Declaration of Helsinki.

Table 2: The antibiotic consumption (Vancomycin, Meropenem, Piperacillin-tazobactam, Ceftazidime and Ceftriaxone) before and during COVID-19 pandemic as measured by DDD per 1000 patient days in HQEII

Antibiotics	DDD Before COVID-19 Pandemic (2018 & 2019)	During COVID-19 Pandemic (2020 & 2021)	% of Change	P-value
Vancomycin	6.85	14.23	+107.75	<0.001
Meropenem	19.59	43.18	+120.40	<0.001
Piperacillin-Tazobactam	49.50	67.51	+36.39	0.003
Ceftazidime	39.09	65.19	+66.79	<0.001
Ceftriaxone	58.74	62.28	+6.03	0.579

The number of cases of resistant organisms before and during pandemic were obtained through the microbiology department report. The multidrug-resistant organisms included in this study were methicillin-resistant *Staphylococcus aureus* (MRSA), *Acinetobacter* sp. MDR, extended spectrum beta lactamases-producing organism (ESBL), Carbapenem-resistant Enterobacterales (CRE) and Carbapenem-resistant *Pseudomonas*.

Statistical analysis

The data was analysed using SPSS version 19. Descriptive analysis, i.e., number and percentage, was used to describe the antibiotic consumption, antibiotic-acquired cost and cases of multidrug resistance

RESULTS

Data was analysed for the period of January 2018 to December 2021. There were 60412 registered patients on the selected antibiotics in 2018 increasing to 61,074, 65,573, 80,894 in 2019 until 2021 respectively.

Antibiotic consumption

The antibiotic consumption showed an overall significant increase of 45.2% (34.8 vs 50.5, p<0.001) during the pandemic. The antibiotic consumption before and during COVID-19 pandemic are shown in Table 2.

Among all departments, Intensive Care Unit (ICU) showed the highest increase

in antibiotic consumption during the pandemic (144.3%). Individually, ICU also showed the highest increase in consumption

for Vancomycin (1749.7%), Piperacillin-tazobactam (109.2%) and Ceftriaxone (70.8%). Interestingly, orthopaedics showed the

Table 3: The comparison of antibiotic consumption as measured by DDD per 1000 patient days before and during COVID-19 pandemic among different departments in HQEII

Department	DDD Before COVID-19 Pandemic (2018 & 2019)	During COVID-19 Pandemic (2020 & 2021)	% of Change	P-value
ICU				
Vancomycin	1.55	28.61	+1749.70	<0.001
Meropenem	71.02	192.53	+171.09	<0.001
Piperacillin-Tazobactam	76.81	160.70	+109.22	<0.001
Ceftazidime	19.30	64.00	+231.63	<0.001
Ceftriaxone	45.94	78.48	+70.83	0.044
Overall	42.92	104.86	+144.30	<0.001
Medical-based				
Vancomycin	3.93	10.57	+168.67	0.002
Meropenem	25.37	55.98	+120.68	<0.001
Piperacillin-Tazobactam	52.26	68.98	+31.48	0.007
Ceftazidime	67.76	116.53	+71.96	<0.001
Ceftriaxone	89.77	116.58	+29.87	0.035
Overall	47.81	73.73	+54.18	<0.001
Surgical-based				
Vancomycin	3.35	12.41	+270.59	<0.001
Meropenem	10.96	36.16	+229.79	<0.001
Piperacillin-Tazobactam	46.43	54.10	+16.53	0.327
Ceftazidime	5.76	21.49	+273.31	<0.001
Ceftriaxone	52.89	45.27	-14.42	0.445
Overall	23.88	33.89	+41.91	0.002
Orthopaedic				
Vancomycin	21.68	18.74	-13.55	0.654
Meropenem	4.23	14.99	+254.66	<0.001
Piperacillin-Tazobactam	41.83	73.91	+76.69	<0.001
Ceftazidime	8.80	47.16	+436.15	<0.001
Ceftriaxone	9.87	7.01	-28.99	0.527
Overall	17.28	32.36	+87.28	<0.001

highest increase for Ceftazidime (436.2%) and Meropenem (254.7%).

Cost of antibiotic consumption

The total cost of antibiotic consumption before COVID-19 pandemic was RM909,898.80 and later increased by 63.2% to RM1,486,791.20 during COVID-19 pandemic. Moving to individual antibiotics, Meropenem showed the highest increase in cost (140.98%), followed by Vancomycin (89.12%), Ceftazidime (89.12%), Piperacillin-tazobactam (43.69%) and Ceftriaxone (16.36%). The total cost of antibiotics used are shown in Table 4.

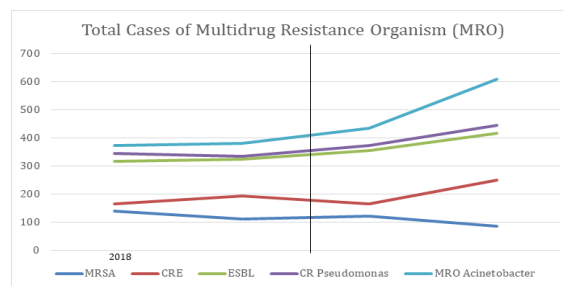


Figure1: The total cases of multidrug resistance organism before and during COVID-19 pandemic

Table 4: The comparison of total cost of antibiotics used before and during COVID-19 pandemic

Types of antibiotics	Total cost of antibiotics used (RM)			
	Before COVID-19 Pandemic (2018 & 2019)	During COVID-19 Pandemic (2020 & 2021)	% of change	P- value
Piperacillin-Tazobactam	218,854.40	314,478.70	+43.69	<0.001
Ceftazidime	206,698.15	364,395.60	+76.29	<0.001
Vancomycin	87,374.40	165,246.50	+89.12	<0.001
Ceftriaxone	251,936.40	293,159.00	+16.36	0.006
Meropenem	145,035.45	349,511.40	+140.98	<0.001
Overall	909,898.80	1,486,791.20	+63.40	<0.001

Bacterial resistance pattern

There were increases in total cases of MRO Acinetobacter, Carbapenem-resistant Pseudomonas, ESBL (*K. pneumoniae*, *K. oxytoca*, *E. coli* & *Proteus Mirabilis*) and Carbapenem-resistant Enterobacterales. However, the total cases of Methicillin-resistant *Staphylococcus aureus* (MRSA) showed a decreasing trend during COVID-19 pandemic. The total cases of multidrug resistance organism are shown in Figure 1.

DISCUSSION

During COVID-19 pandemic, all of the selected antibiotic consumption, except Ceftriaxone, showed a significant increase in HQEII.

Specifically, Meropenem showed the highest increase in consumption among all antibiotics. Among all departments, ICU showed the highest increase in antibiotic consumption particularly for Vancomycin, Piperacillin-tazobactam and Ceftriaxone. Similar findings were observed in Spain with 11.5% increment on antibiotic use during Covid-19 pandemic (Gonzalez-Zorn, 2021). A study by Silva ARO et al observed similar outcome in ICU settings for Brazilian hospitals with the overall antimicrobial consumption increased from January-2019 to December-2020 by 11.2% (Silva et al., 2021). ICU is catered for critically ill patients, including those with severe bacterial infections, which may explain its high consumption of antibiotics. However,

the indication for the use of each antibiotic was not explored in this study. Hence, while there was an obvious increasing trend during the COVID-19 pandemic, the rationale for high consumption of these antibiotics was unclear.

The significant increase in antibiotic consumption during the COVID-19 pandemic also led to a significant increase in total cost of antibiotics by 63.2%. Meropenem contributed with the highest increase in cost. Reducing the consumption of antibiotics can be a measure to lower the cost of antibiotics use. This can be done by de-escalating these antibiotics to a less expensive narrow-spectrum antibiotic and by reducing the duration of antibiotic therapy (Cheah et al., 2021).

With the increased consumption of antibiotics, there were also increases in total cases of multidrug resistant organisms (MRO), especially MRO *Acinetobacter* and Carbapenem-resistant *Enterobacterales*. Similar increase in MRO cases was also observed in an acute care hospital in Brazil, whereby the overall incidence of multidrug resistance (MDR) infections increased by 23% ($P < .005$) during COVID-19 (Polly et al., 2022). Interestingly, there was a disproportionate MRSA case even with an increase in vancomycin usage. As mentioned earlier, the rationale of high antibiotic consumption was not explored in this study to fully understand the correlation between antibiotic consumption and multidrug resistant organisms. It is widely agreed that the overuse of antibiotics is the main driver in the development of antimicrobial resistance. However, other factors such as the misuse of antibiotics, i.e., inappropriate antibiotic choice and duration, may also play a role in accelerating antimicrobial resistance (Antimicrobial Resistance, n.d.).

HQEII was designated as the main non-COVID-19 referral centre in west coast Sabah during the pandemic. Some sub-specialities from COVID-19 hospitals were transferred to HQEII, increasing the patient load by a bed

occupancy rate of 7.4%. Also, patients referred to HQEII from other facilities were generally in a more severe disease state. This may lead to an increase in antibiotic consumption during the pandemic.

Earlier in the year 2017, Antimicrobial Stewardship (AMS) programme was introduced in HQEII to enforce the appropriate use of optimal antimicrobial drug regimen. During COVID-19 pandemic, there was an interruption of AMS service which was carried out twice weekly and the round was withheld from March 2020 until October 2021. The AMS team was also redeployed to manage the pandemic, resulting in the lack of antibiotic surveillance. Similar to previous literature findings, the results of this study suggest that AMS programme is imperative towards the vigilant use of antibiotics and to combat antimicrobial resistance (Elshenawy et al., 2023).

CONCLUSION

High antibiotic consumption, antibiotic-acquired cost and multidrug resistance organism (MRO) cases were observed in non-COVID-19 healthcare setting during the pandemic. However, the factors contributing to the surge were not explored in this study. Our suggestion for future studies would be to include the factors contributing to antibiotic consumption as well as the bacterial resistance pattern.

DECLARATION OF INTEREST

The authors declare no conflict of interest.

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