

Original Article

Comparing the appropriateness of antimicrobial prescribing among medical patients in two tertiary hospitals in Malaysia

Ly Sia Loong¹, Pauline Siew Mei Lai¹, Nurul Adilla Hayat Jamaluddin^{2,3}, Isa Naina-Mohamed², Petrick Periyasamy⁴, Chee Lan Lau^{2,5}, Karin Thursky⁶, Rodney James⁶, Sasheela Ponnampalavanar⁷, on behalf of The Malaysian NAPS Working Group

¹ Department of Primary Care Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia ² Pharmacoepidemiology and Drug Safety Unit, Department of Pharmacology, Faculty of Medicine, Universiti Kebangsaan Malaysia, Cheras, Kuala Lumpur, Malaysia

³ Department of Hospital and Clinical Pharmacy, Faculty of Pharmacy, University of Cyberjaya, Cyber 11, Cyberjaya, Selangor, Malaysia

⁴ Medical Department, Faculty of Medicine, Universiti Kebangsaan Malaysia, Cheras, Kuala Lumpur, Malaysia

⁵ Pharmacy Department, Hospital Canselor Tuanku Muhriz, Cheras, Kuala Lumpur, Malaysia

⁶ National Centre for Antimicrobial Stewardship (NCAS), University of Melbourne and Royal Melbourne Hospital, Australia

⁷ Department of Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

Abstract

Introduction: Malaysia is an upper-middle-income country with national antimicrobial stewardship programs in place. However, hospitals in this country are faced with a high incidence of multidrug-resistant organisms and high usage of broad-spectrum antibiotics. Therefore, this study aimed to use a standardized audit tool to assess clinical appropriateness, guideline compliance, and prescribing patterns of antimicrobial use among medical patients in two tertiary hospitals in Malaysia to benchmark practice.

Methodology: A prospective hospital-wide point prevalence survey was carried out by a multidisciplinary team in April 2019 at the University Malaya Medical Centre (UMMC) and the Hospital Canselor Tuanku Muhriz (HCTM), Kuala Lumpur, Malaysia. Data was collected from the patient's electronic medical records and recorded using the Hospital National Antimicrobial Prescribing Survey toolkit developed by the National Centre for Antimicrobial Stewardship, Australia.

Results: The appropriateness of prescriptions was 60.1% (UMMC) and 67% (HCTM), with no significant difference between the two hospitals. Compliance with guidelines was 60.0% (UMMC) and 61.5% (HCTM). Amoxicillin-clavulanic acid was the most commonly prescribed antimicrobial (UMMC = 16.9%; HCTM = 11.9%).

Conclusions: The appropriateness of antimicrobial prescribing in medical wards, compliance with guidelines, and prescribing patterns were similar between the two hospitals in Malaysia. The survey identified several areas of prescribing that would need targeted AMS interventions.

Key words: Antimicrobial stewardship; hospital; appropriateness.

J Infect Dev Ctries 2022; 16(12):1877-1886. doi:10.3855/jidc.15925

(Received 29 March 2022 - Accepted 16 May 2022)

Copyright © 2022 Loong *et al.* This is an open-access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Introduction

Malaysia is an upper-middle-income country with broad adoption of antimicrobial stewardship (AMS) programs in hospitals [1]. The University Malaya Medical Centre (UMMC) and the Hospital Canselor Tuanku Muhriz (HCTM) are two tertiary hospitals located in Kuala Lumpur, Malaysia. These hospitals face increasing rates of hospital-acquired multidrugresistant organisms (MDROs), while facing challenges in compliance with infection prevention and control guidelines and appropriate usage of antimicrobials [2]. In a 2016 survey, both hospitals were among the top five hospitals in the country with the highest carbapenem usage (mean utilization of 50 Defined Daily Dose (DDD)/1000 patient days) [1].

The establishment of an AMS team is a requirement for all public and large private hospitals in Malaysia and is a key performance index (KPI) under the Malaysian Patient Safety Goal [1]. Both the UMMC and the HCTM have established AMS teams and interventions such as hospital antimicrobial prescribing guidelines, post-prescription review of selected antibiotic prescriptions by pharmacists with prescriber feedback, implementation of carbapenem pre-order form and AMS rounds targeting selected wards or antibiotics since 2015. However, the effectiveness of these interventions has not been objectively measured in a standardized and sustainable way.

The effectiveness of AMS programs may be assessed by structural, process, and outcome measures [3]. Structural measures such as the availability of facilities and expertise would not reflect the effectiveness of interventions, while clinical outcome measures such as mortality are mostly recommended to ensure interventions do not have unintended consequences [3]. Measurement of the burden of antimicrobial use such as DDD per 100 patient days, is commonly used but cannot immediately inform inappropriateness of use, and are also not suitable for pediatrics [4]. Compliance with guidelines is a widely used process measure [3] but often does not reflect reallife multifaceted patient scenarios that require clinical judgment [5]. measures of clinical Process appropriateness of antimicrobial use (which evaluates the choice of agent, dosage, duration, allergies, drug interactions, toxicities, and documentation) are the best method as a proxy to indicate improvements in practice [5]. However, ways to measure clinical appropriateness in a reliable, standardized, and widely accepted manner are still a matter of debate [6]. National Action Plans for AMR recommend regular monitoring of the quality of antimicrobial use [3,7-9] but do not include gold standards for clinical appropriateness. Benchmarking allows for evaluation of the quality of antimicrobial use against other similar institutions and enables a measure of "best practice".

The Australian National Antimicrobial Prescribing Survey (NAPS) (Guidance Group, Royal Melbourne Hospital) is a well-established web-based auditing platform used to assess the guideline compliance and appropriateness of antimicrobial use. The NAPS was designed for use by multidisciplinary healthcare professionals across different healthcare institutions. This tool assists facilities identify KPIs and allow hospitals to benchmark their results in real-time against other participating hospitals in a standardized and meaningful way, according to hospital type, case mix, size, and location. The online Hospital NAPS tool has been available in Australia since 2013, with over 600 (62%) of all public and private hospitals participating across all states and territories nationwide [10]. Data collected have been utilized at a local, jurisdictional and national level to inform strategies to improve the quality of antimicrobial prescribing within Australian Hospitals, and findings have contributed to the Antimicrobial Use and Resistance in Australia (AURA) surveillance system [11].

Antimicrobials are commonly prescribed in the medical wards [12-15], in both developing and developed countries, with medical wards showing antimicrobial use ranging from 45%-69% of total antimicrobial consumption per institution [13–15]. The reported appropriateness of antimicrobial prescribing in medical wards varies greatly depending on the economic status of the region studied and the maturity of the AMS program (19%- 67.1%) [16-19]. A pilot study using the Hospital NAPS tool in selected medical wards (geriatric, dermatology, general medicine) in the UMMC found that the appropriateness of antimicrobial prescriptions was 61.1% (11/17). In contrast, Australian Hospital NAPS data reported an appropriateness of 77.6% in a comparable patient group [10]. Therefore, this study aimed to undertake the NAPS to assess the generalizability, and feasibility in the Malaysian hospital setting, and to assess the clinical appropriateness, guideline compliance, and prescribing patterns of antimicrobial use among medical patients in two tertiary hospitals in Malaysia in order to benchmark practice.

Methodology

Study design, setting, and period of study

A prospective hospital-wide point prevalence survey (PPS) was conducted in the UMMC and the HCTM [20], in Kuala Lumpur, Malaysia between 22 and 30 April 2019. Both hospitals are similar in their size and services offered; with 1,617 beds and 44 wards in the UMMC, and 1,054 beds and 63 wards in the HCTM. The medical departments from both hospitals have similar sub-specialties such as cardiology, respiratory, nephrology, gastroenterology, geriatric, dermatology, endocrine, hematology, bone marrow transplant, and infectious diseases. Approval from the ethics committee of UMMC and HCTM (the UMMC: MREC ID No: 201924-7101 and HCTM: JEP 2019-245) was obtained before the commencement of this study.

The auditing team

A multidisciplinary team consisting of one pharmacist and four Infectious Diseases physicians in the UMMC; nine pharmacists, and two Infectious Diseases physicians in the HCTM participated in the survey. The NAPS support team provided resources and training for the collection of audit data prior to the commencement of the audits. All auditors viewed twelve online training videos followed by an eLearning assessment, where at least one auditor from each team was required to score at least 80% before being able to finalize patient data.

Outcomes measured

The primary outcome was to assess the appropriateness of antimicrobial use among medical patients. The secondary outcome was to assess compliance with guidelines, and prescribing patterns of antimicrobial prescriptions, and to compare practice between two tertiary teaching hospitals in Malaysia.

Operational definitions

Antimicrobials are defined as antibacterial, antifungals, antivirals, anti-tuberculosis, antimalaria, antiprotozoals, and intraluminal antibiotics. These included antimicrobials prescribed for prophylaxis or treatment of an infection.

Inclusion and exclusion criteria

All patients that were admitted to a medical ward who were prescribed an antimicrobial by any route of administration (intravenous, oral, rectal, inhalation, or topical) at 8 am on the designated audit day or received surgical prophylaxis in the 24 hours prior were included. As previously described, outpatients, daycare, and non-admitted emergency department patients were excluded [10].

Instruments used

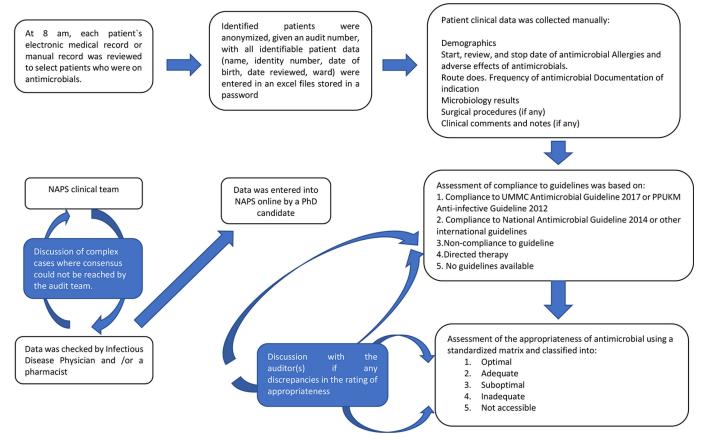
Hospital National Antimicrobial Prescribing Survey (Hospital NAPS)

The Hospital NAPS comprises of a survey pack including a user guide, a data collection form, an appropriateness assessment matrix [10,11], and worked case examples. For this study, a new data entry portal, specific to Malaysia, was created on the existing NAPS online platform. This allowed for the registration of the participating facilities and auditors, and the entry of the audit data into a secure database. Prior to data entry, minor technical updates were introduced, including adding new specialties and antimicrobials to the database. Terminology for indications was updated in the list of medical indications used in the Hospital NAPS

Guidelines used

The UMMC and the HCTM both have hospital antimicrobial prescribing guidelines developed by their

Figure 1. Data Collection Process.



respective infectious diseases units and pharmacists, in collaboration with individual sub-specialties [21,22]. These guidelines were used as primary references in UMMC and secondary references in HCTM.

The National Antibiotic Guidelines 2014, published by the Malaysian Ministry of Health in 2014 was used as secondary references in UMMC and primary references in HCTM [23,24].

Data collection process

Data was collected as described in Figure 1. In the UMMC, progress notes and electronic prescribing records were used for assessment, whilst in the HCTM only manual progress notes were used. When there was discrepancies or ambiguous documentation in electronic prescription and/or progress notes, indication in progress notes were taken as a point of reference. Clinical appropriateness was assessed based on the standardized appropriateness matrix by a pharmacist (LSL, NAHJ) and an Infectious Disease physician (HCO, RXN, AK, AS, NK) in each facility. If the team could not come to a consensus regarding the case, a more senior Infectious Diseases physician (SP, PP) of each hospital or the Australian NAPS clinical support team (RJ) was consulted.

Data analysis

Data was analyzed using Statistical Package for Social Science (SPSS) version 20.0 software (Chicago, Illinois, USA). Normality was tested using the Kolmogorov-Smirnov test. Data was found to be not normally distributed. Hence, categorical variables were presented as percentages and frequencies, whilst continuous variables were presented as median and interquartile range. The difference between the two centers was analyzed by using the Chi-square test or Fisher's exact test (if the minimum expected count was < 5) for categorical variables, and the Mann-Whitney was used for continuous variables. A *p* value < 0.05 was determined as statistically significant.

Results

A total of 260 patients on 372 antimicrobial prescriptions from both centers were included in the analysis. The prevalence of antimicrobial use in selected medical wards was 49.5% (139/281) and 57.3% (121/211), in the UMMC and the HCTM, respectively. The median age of patients in the UMMC was 62 years (43.5-75.0) and in the HCTM was 65 years (49.0-74.0). No significant difference was found in the demographic characteristics of patients from both hospitals.

Most common specialty

In both centers, the general medicine specialty had the highest usage of antimicrobials (Table 1). The specialty with the lowest antimicrobial used was Infectious Disease in the UMMC and Cardiology in the HCTM. There was no significant difference in the number of antimicrobials prescribed in the different medical specialties, except that the Cardiology (p <

Table 1. Most common specialty, site of infection for prescribing antimicrobials and most common antimicrobials prescribed.

Danking	Most common specialty			
Ranking	UMMC $(n = 178)$ (%, n)	HCTM $(n = 194)$ (%, n)	<i>p</i> value	
1	General Medicine# (54.5%, 97)	General Medicine# (61.3%,119)	0.181	
2	Haematology (14.6%, 26)	Haematology (22.2%, 43)	0.061	
3	Cardiology (11.8%, 21)	Cardiology (2.1%, 4)	< 0.001*	
4	Nephrology (10.1%, 18)	Nephrology (9.3%, 18)	0.786	
5	Infectious disease (9.0%, 16)	Infectious disease (5.2%, 10)	0.147	
Ranking	Most common site of infection			
	UMMC (n = 178) (%, n)	HCTM (n = 194) (%, n)		
1	Respiratory (28.7%,51)	Respiratory (36.6%,71)	0.103	
2	Sepsis and bacteraemia (14.6%, 26)	Sepsis and bacteraemia (12.4%, 24)	0.528	
3	Medical prophylaxis (10.7%, 19)	Medical prophylaxis (16%, 31)	0.134	
4	Other (10.1%, 18)	Other (2.6%, 5)	0.004*	
5	Systemic infection (7.3%, 13)	Systemic infection (5.7%, 11)	0.522	
6	Skin and soft tissue infection (7.3%, 13)	Skin and soft tissue infection (6.2%, 12)	0.667	
Ranking	Most common antimicrobials prescribed (%, n)			
1	Amoxicillin – clavulanic acid (16.9%, 30)	Amoxicillin – clavulanic acid (11.9%, 23)	0.168	
2	Piperacillin – tazobactam (12.4%, 22)	Piperacillin – tazobactam (9.8%, 19)	0.430	
3	Ceftriaxone (5.1%, 9)	Ceftriaxone (10.8%, 21)	0.041*	
4	Fluconazole (5.1%, 9)	Fluconazole (3.6%, 7)	0.492	
5	Cloxacillin (4.5%, 8)	Cloxacillin (3.1%, 6)	0.478	

*Statistically significant at p < 0.05; #General medical wards consist of endocrinology, gastroenterology, respiratory, dermatology, neurology, rheumatology, palliative care; N/A: Not applicable; UMMC: University Malaya Medical Centre; HCTM: Hospital Canselor Tuanku Muhriz.

0.001) in the UMMC prescribed significantly more antimicrobials compared to the HCTM.

Most common site of infection (indication)

The five most common sites of infection for prescribing antimicrobials in the UMMC compared to the HCTM are listed in Table 1. Respiratory tract infections were the most common sites in both centers, with the majority consisting of pneumonia, 78.4% (40/51) cases in the UMMC and 77.5% (55/71) in the HCTM respectively.

Most common antimicrobials

The five most common antimicrobials prescribed in the UMMC compared to the HCTM are listed in Table 1. The prescribing pattern for antimicrobials was similar in both centers, with amoxicillin-clavulanic acid being the most frequently prescribed antimicrobial. However, the HCTM showed significantly higher usage of ceftriaxone (p = 0.041) compared to the UMMC.

Compliance with guidelines

There was no significant difference in rates of compliance with guidelines between the two centers. Combined compliance was 60.8% (180/296), with the UMMC reporting 60.0% (78/130) and the HCTM 61.5% (102/166) respectively. These figures excluded antimicrobials that were classified as "directed therapy", "not assessable" and "no guideline available". Prescriptions that were used as "directed therapy" (p = 0.006) and "not assessable" (p = 0.016) were significantly higher in the UMMC compared to the HCTM. Prescriptions could not be assessed because indication for antimicrobial use was not documented.

Appropriateness of antimicrobial prescriptions

There was no significant difference in the overall rates of appropriateness between the two centers. The

combined appropriateness from both centers was 63.7% (237/372; optimal 54.6% and adequate 9.1%). In the UMMC 60.1% (107/178; optimal 51.1% and adequate 9.0%) prescriptions were appropriate and 67% (130/194; optimal 57.7% and adequate 9.3%) in the HCTM. However, the UMMC had significantly more sub-optimally (p = 0.037) prescribed antimicrobials compared to the HCTM. In both centers, the majority

compared to the HCTM. In both centers, the majority of "directed therapy" were rated as appropriate at 85% (28/33) in the UMMC and 82% (14/17) in the HCTM.

Respiratory site infections had lower rates of appropriateness compared to sepsis and medical prophylaxis in both centers. Only 52.6% (20/38) and 54.5% (30/55) of antimicrobials used for pneumonia were appropriate in the UMMC and the HCTM, respectively.

The rate of appropriateness was analyzed for the three most common medical specialties, sites of infection, and antimicrobials as listed in Table 2. In the UMMC, Hematology and the use of antimicrobials as medical prophylaxis had a significantly lower rate of appropriateness compared to the HCTM. In the UMMC, a majority (42.3%, 11/26) of prescriptions for Hematology were used for medical prophylaxis in immunocompromised patients.

Reasons for inappropriate prescriptions

Suboptimal appropriateness was due to a significantly higher number of prescriptions with an 'incorrect duration' and 'spectrum too narrow' in the UMMC compared to the HCTM. An 'Incorrect duration' was mainly found in prescriptions for empiric use for pneumonia (n = 5), sepsis (n = 3), and cystitis (n = 2). 'Spectrum too narrow' was mainly found in prescriptions for empiric use for pneumonia (n = 8) where the severity of infection warranted a macrolide but was not prescribed [21].

	UMMC $(n = 178)$ (%, n)	HCTM $(n = 194)$ (%, n)	<i>p</i> value
Specialty			
General Medicine#	59.8%, 58/97	63%, 75/119	0.218
Haematology	50%, 13/26	83.7%, 36/43	0.004*
Cardiology	47.6%, 10/21	25%, 1/4	0.604
Site of Infection			
Respiratory	52.9%, 27/51	59.2%, 42/71	0.495
Sepsis and bacteraemia	73%, 19/26	75.0%, 18/24	0.877
Medical prophylaxis	73.4%, 14/19	96.8%, 30/31	0.015*
Antimicrobials			
Amoxicillin – clavulanic acid	40%, 12/30	60.9%, 14/23	0.132
Piperacillin – tazobactam	59.1%, 13/22	36.8%, 7/19	0.155
Ceftriaxone	44.4%, 4/9	47.6%, 10/21	0.873

*Statistically significant at *p* < 0.05; #General medical wards consist of endocrinology, gastroenterology, respiratory, dermatology, neurology, rheumatology, palliative care; UMMC: University Malaya Medical Centre; HCTM: Hospital Canselor Tuanku Muhriz.

Table 3 showed that 'Incorrect duration' (p = 0.017)and 'Spectrum too narrow' (p = 0.030) was the top reason prescriptions were inappropriate in the UMMC and the HCTM respectively. Prescriptions where 'antimicrobials not indicated' (p = 0.003) were significantly higher in UMMC compared to the HCTM. 'Antimicrobials not indicated' in the UMMC were prescribed for non-infectious indications (n = 4) like eye-toilet, medical prophylaxis of mucositis (n = 2), and in upper respiratory tract infections (n = 2).

Documentation

A documented indication for the use of antimicrobials were present in 89.9% (160/178) of prescription in the UMMC and 85.1% (165/194) in the HCTM (p = 0.161). Documentation of stop or review date was significantly higher (p < 0.001) in the UMMC (93.8%, 167/178) compared to the HCTM (41.8%, 81/194).

Discussion

Comparing and contrasting antimicrobial prescribing practices between two medical centers in Malaysia has provided insights to guide AMS initiatives. Though the prescribing quality for antimicrobials in both centers was acceptable, there were several targets for quality improvement initiatives identified.

The prevalence of antimicrobial use in our study UMMC 49.5%; HCTM 57.3%) was lower when compared to studies in other Asian countries such as Indonesia (84%) [18], and Pakistan (82.3%) [25], but similar to a study which involved 20 hospitals across Europe (19%-59%) [26]. However, the prevalence of antimicrobial use does not necessarily reflect the appropriateness of prescribing and could instead be more reflective of the acuity or case mix of admitted patients and the changing antibiotic resistance patterns within a healthcare setting [27]. Therefore, caution is

needed when comparing the prevalence between facilities.

A superior indicator would be the rate of standardized appropriateness for antimicrobial prescribing. The rate of appropriateness was similar between the two centers; however, the combined rates (63.7%) were lower when compared to the medical cohort in Australian hospitals (77%) [11], using the same appropriateness assessment tool (Hospital NAPS). One possible reason for this is that AMS programs are still in the early stages of implementation in Malaysia, only being included as a KPI for hospitals in 2017 under the Malaysia Action Plan for Antimicrobial Resistance (MyAP-AMR) [1], whereas in 2011 the Australian Commission on Safety and Quality in Health Care (ACSOHC) had developed guidelines for essential AMS activities, which became accreditation standards for all Australian hospitals [28]. This highlights the importance of benchmarking against other facilities using the same assessment tool to make meaningful comparisons that can be used to set standards and targets for KPIs.

Findings from our study provide evidence for the need to improve antimicrobial prescribing in pneumonia as the rates of appropriateness were low in both centers. This is in line with recommendations by the Centers for Disease Control and Prevention (CDC) that community-acquired pneumonia is included as a core element of any AMS initiative because it is one of the most common infections encountered in a clinical setting. These initiatives may include confirmation of an infectious diagnosis and severity of illness, avoiding empiric use of antipseudomonal beta-lactams or Methicillin-resistant *Staphylococcus aureus* (MRSA) agents [29], and promoting the use of five days of treatment for uncomplicated pneumonia [30].

Prescribing antimicrobials for an incorrect duration and when not indicated was significantly more frequent in the UMMC compared to the HCTM. Though the optimal antimicrobial duration has long been arbitrary,

 Table 3. Reasons for inappropriate antimicrobial prescriptions in the University Malaya Medical Centre and the Hospital Canselor Tuanku Muhriz.

	UMMC and HCTM (n = 135) (%, n)	UMMC (n = 58) (%, n)	HCTM (n = 56) (%, n)	<i>p</i> value ^a
Allergy mismatch	1.5%, 2	3.4%, 2	0	0.496 ^b
Microbiology mismatch	2.2%, 3	1.7%, 1	3.6%, 2	0.615 ^b
Incorrect route	6.7%, 9	5.2%, 3	10.7%, 6	0.317 ^b
Incorrect dose and/or frequency	23.7%, 32	24.1%, 14	32.1%, 18	0.342
Incorrect duration	14.8%, 20	25.9%, 15	8.9%, 5	0.017*
Spectrum too broad	20.0%, 27	20.7%, 12	26.8%, 15	0.444
Spectrum too narrow	25.2%, 34	20.7%, 12	39.3%, 22	0.030*
Antimicrobials not indicated	11.1%, 15	22.4%, 13	3.6%, 2	0.003*

*Statistically significant at *p* < 0.05; *Chi-Squared, *Fisher Exact test; UMMC: University Malaya Medical Centre; HCTM: Hospital Canselor Tuanku Muhriz

based on anecdotal data and expert opinion [31], current evidence supports shorter duration of treatment for many common infections such as uncomplicated urinary tract infection for three days [32], communityacquired pneumonia for five days [33], and ventilatorassociated pneumonia for eight days [34]. Both prolonged duration and unnecessary use of antimicrobial has been shown to increase the emergence of antimicrobial-resistant organisms with adverse effects and incurs higher costs [31,35–38]. AMS initiatives focusing on improving these two areas should be considered in the UMMC.

In the HCTM, prescribing antimicrobials with incorrect dosage and too narrow a spectrum were the main reasons for inappropriateness. CDC recommends that dose adjustment and optimization are core elements of pharmacy-based AMS interventions [29], and should be considered as a priority in the HCTM. Though this study did not investigate in-depth the reasons why antimicrobials prescribed were too narrow a spectrum, pneumonia was the main indication that was inappropriately prescribed and these were not compliant with guidelines. This could be due to insufficient coverage in the treatment of moderate to severe pneumonia that warrants further investigation in the HCTM.

Similar to the results from our study, the lack of documentation was reported in other studies in North Africa (59.2%) [39], and the United Kingdom (37%) [40]. Documentation of indication is shown to be an evidence-based method of reducing inappropriate antimicrobial prescribing [41] and is a key recommendation in Malaysia's National AMS policies [8]. A study in a respiratory ward in the United Kingdom that utilized Plan-Do-Study-Act (PDSA) method found that an intervention bundle improved documentation of indications (including severity scores) and also compliance with antimicrobial guidelines [41]. Other AMS interventions that have been shown to improve documentation were the use of indication-enabled decision support [42,43], a computerized antimicrobial approval system [44], and the creation of a separate section for antimicrobial prescribing in the medical records [40]. We stand to benefit by learning from and possibly implementing similar or modified intervention bundles in our setting.

Other areas that warrant further evaluation and possible improvement are the antimicrobial prescribing practice is in the Cardiology and Hematology specialty at the UMMC. Cardiology showed significantly higher usage than a parallel specialty in the HCTM, with rates of appropriate antimicrobial use (47.6%) lower than the

hospital-wide average (60.1%). No studies specifically explored the reason for inappropriate use in Cardiology, but in the UMMC, pneumonia was the most common inappropriate indication, and amoxicillin-clavulanic acid was the most common inappropriate antimicrobial used. Hematology in the UMMC showed lower rates of appropriateness compared to the HCTM. The most common inappropriate indication was fungal and viral prophylaxis in immunocompromised patients with the most common inappropriate antimicrobial being acyclovir and nystatin. The appropriate use of antimicrobial prophylaxis in this group of patients has also been highlighted as an area that needs improvement in Hematology units across Australia [45].

Amoxicillin–clavulanic acid was found to be the most commonly used antimicrobial in both centers according to hospital guidelines. Though amoxicillinclavulanic falls under the "Access" group of antibiotics by WHO's AWaRe classification because of its comparatively lower resistance potential than other antibiotics in the "Watch" or "Reserve" group [46], it remains a broad-spectrum antibiotic and should not be prescribed where narrower antibiotics would suffice [47]. Therefore, the high usage in both centers should raise caution for further investigations. Combined compliance to antimicrobial guidelines from both centers (60%) was also comparable to the Hospital NAPS data from Australia (67.3%) [11] and other European studies (67%-77.3%) [48,49].

The results of this study were presented to hospital management and clinical teams. This drove discussions with specialists to design AMS initiatives. However, the success of any AMS intervention is dependent on its ability to change the behavior of prescribers [50], therefore, a qualitative study will also be done to understand the barriers and facilitators in implementing AMS interventions. Intervention bundles will then be implemented based on both quantitative findings from this study and qualitative results. This study has also helped the centers to improve upon their guidelines and new versions have since been published. The UMMC has also adopted the Hospital NAPS as a tool to annually assess the quality of antimicrobial prescribing.

The strength of our study was that we used a standardized and validated tool, the Hospital NAPS, to assess antimicrobial appropriateness, compliance, and prescribing patterns in medical wards. This allowed for a more objective and consistent assessment and subsequent comparison between centers and even countries that used the same toolkit. This study also demonstrated the successful adaptation of an Australian-developed assessment toolkit in our local setting, while still ensuring consistency and standardization in implementation across the two centers. This was done through online meetings with the NAPS support team to allow for a question-andanswer session on the assessment tool and the data collection process. Particularly helpful in ensuring standardized assessment was the appropriateness assessment matrix, which was easy to use, feasible in our setting, and able to be undertaken by our trained auditors. This study showed the adaptability, feasibility, and potential generalization of Hospital NAPS tools to wider usage in other settings. In addition, two centers in Malaysia were involved in this study, which allowed for a comparison of practice. Through this study, a better understanding of the quality and prescribing patterns of antimicrobials in each center was achieved and areas for future AMS interventions were identified.

One of the limitations of this study was that comparison could only be done with one other center in our setting that used the same assessment tool. A larger pool of data would allow for more in-depth analysis and should be considered for future studies. Direct comparison with other studies that used different assessment tools was also difficult.

Conclusions

Overall, the appropriateness of antimicrobial prescribing in medical wards, compliance with guideline, and the prescribing pattern was similar between the two tertiary teaching hospitals in Malaysia, but a few areas in need of improvement were identified at both centers. Targeted areas that were identified for further evaluation and AMS interventions were antimicrobial use for pneumonia, appropriateness of dosage, indication, duration, and quality of documentation. Specific specialties such as antimicrobial use in Cardiology and Hematology may also warrant further investigation. It will be beneficial in the future to compare appropriateness to other hospitals within the Asia-Pacific region as more countries use the NAPS platform for auditing their antimicrobial prescribing practices.

Acknowledgements

The Malaysian NAPS Working Group: Adeeba Kamarulzaman, Sharifah Faridah Syed Omar, Asma Sohail, Pui Li Wong, Bushra Megat Johari, Hang Cheng Ong, Rong Xiang Ng, Anjanna Kukreja, Mia Tuang Koh, Lay Teng Tan, Ching Hooi Tan, Chuey Ee Lee, Ka Yin Lim, Mei Kuan Yin, Nur Jannah Azman, Najma Kori, Ramliza Ramli, Toh Leong Tan. Pfizer Independent Grants for Learning and Change (IGLC) provided all project funding and The Joint Commission provided administrative oversight for this program. Funding (Grant No:40867041) was received by Dr Sasheela Ponnampalavanar, the corresponding author. We thank our colleagues from University Malaya Medical Centre, University Kebangsaan Malaysia, and National Centre for Antimicrobial Stewardship who provided insight and expertise that greatly assisted the research.

References

- Ministry of Health and Ministry of Agriculture and Agro-Based Industry Malaysia (2017) Malaysian action plan on antimicrobial resistance (MyAP-AMR) 2017-2021. Available: https://www.moh.gov.my/moh/resources/Penerbitan/Garis Panduan/Garis panduan Umum (Awam)/National_Action_Plan_-FINAL_29_june.pdf. Accessed: 5 January 2022.
- Pharmacy Practice and Development Division Ministry of Health (2017) The report on antibiotic utilisation in Malaysian hospitals. https://www.pharmacy.gov.my/v2/sites/default/files/documen t-upload/report-antibiotic-utilisation-malaysian-hospitals-2008-2017.pdf. Accessed: 14 January 2022.
- World Health Organization (2019) Antimicrobial stewardship programmes in health-care facilities in low-and middle-income countries: a WHO practical toolkit. Available: https://www.who.int/publications/i/item/9789241515481. Accessed: 17 January 2022.
- 4. Pulcini C, Hulscher M (2019) How can we routinely measure appropriateness of antimicrobial use in hospitals at a national level? JAMA Netw Open 2: e1915030.
- 5. Morris AM (2014) Antimicrobial stewardship programs: appropriate measures and metrics to study their impact. Curr Treat Options Infect Dis 6: 101–112.
- Spivak ES, Cosgrove SE, Srinivasan A (2016) Measuring appropriate antimicrobial use: attempts at opening the black box. Clin Infect Dis an Off Publ Infect Dis Soc Am 63: 1639– 1644.
- Goff DA, Kullar R, Goldstein EJC, Gilchrist M, Nathwani D, Cheng AC, Cairns KA, Escandón-Vargas K, Villegas MV, Brink A, van den Bergh D, Mendelson M (2017) A global call from five countries to collaborate in antibiotic stewardship: united we succeed, divided we might fail. Lancet Infect Dis 17: e56–e63.
- Ministry of Health Malaysia (2014) Protocol on antimicrobial stewardship program in healthcare facilities. Available: https://www.pharmacy.gov.my/v2/sites/default/files/documen t-upload/protocol-antimicrobial-stewardship.pdf. Accessed: 11 January 2022.
- 9. Davey PG, Marwick C (2008) Appropriate vs. inappropriate antimicrobial therapy. Clin Microbiol Infect 14: 15–21.
- National Centre for Antimicrobial Stewardship and Australian Commission on Safety and Quality in Health Care. Antimicrobial prescribing practice in Australian Hospitals Results of the 2019 Hospital National Antimicrobial Prescribing Survey. Sydney: ACSQHC; 2021
- 11. Australian Commission on Safety and Quality in Health Care (ACSQHC). AURA 2019: third Australian report on antimicrobial use and resistance in human health. Sydney: ACSQHC; 2019.

- 12. Kallen MC, Natsch S, Opmeer BC, Hulscher MEJL, Schouten JA, Prins JM, van der Linden P (2019) How to measure quantitative antibiotic use in order to support antimicrobial stewardship in acute care hospitals: a retrospective observational study. Eur J Clin Microbiol Infect Dis Off Publ Eur Soc Clin Microbiol 38: 347–355.
- Nia SS, Hiremath SRR, Prasad S (2018) Assessment of antimicrobial use pattern using World Health Organization prescribing indicators at a tertiary hospital: A prospective, observational study. J Appl Pharm Sci 8: 132–138.
- 14. Şengel BE, Bilgin H, Bilgin BÖ, Gidener T, Saydam S, Pekmezci A, Ergönül Ö, Korten V (2019) The need for an antibiotic stewardship program in a hospital using a computerized pre-authorization system. Int J Infect Dis 82: 40– 43.
- Gürtler N, Erba A, Giehl C, Tschudin-Sutter S, Bassetti S, Osthoff M (2019) Appropriateness of antimicrobial prescribing in a Swiss tertiary care hospital: A repeated point prevalence survey. Swiss Med Wkly 149: w20135.
- Willemsen I, Groenhuijzen A, Bogaers D, Stuurman A, van Keulen P, Kluytmans J (2007) Appropriateness of antimicrobial therapy measured by repeated prevalence surveys. Antimicrob Agents Chemother 51: 864–867.
- 17. Cusini A, Rampini SK, Bansal V, Ledergerber B, Kuster SP, Ruef C, Weber R (2010) Different patterns of inappropriate antimicrobial use in surgical and medical units at a tertiary care hospital in Switzerland: a prevalence survey. PLoS One 5: e14011.
- Hadi U, Duerink DO, Lestari ES, Nagelkerke NJ, Keuter M, In't Veld DH, Suwandojo E, Rahardjo E, van den Broek P, Gyssens IC (2008) Audit of antibiotic prescribing in two governmental teaching hospitals in Indonesia. Clin Microbiol Infect 14: 698–707.
- Chandrasekhar D, Manaparambil H, Parambil JC (2019) Outcome assessment of intervention on appropriateness of antibiotic use among geriatric patients: A prospective interventional study from a tertiary care referral hospital. Clin Epidemiol Glob Heal 7: 536–541.
- Jamaluddin NAH, Periyasamy P, Lau CL, Ponnampalavanar S, Lai PSM, Ramli R, Tan TL, Kori N, Yin MK, Azman NJ, James R, Thursky K, Naina-Mohamed I (2021) Point prevalence survey of antimicrobial use in a Malaysian tertiary care university hospital. Antibiotics 10: 531.
- Tunger O, Karakaya Y, Cetin CB, Dinc G, Borand H (2009) Rational antibiotic use. J Infect Dev Ctries 3: 88–93. doi: 10.3855/jidc.54.
- 22. University Malaya Medical Center (2020) University malaya medical center antibiotic guideline. Available: https://farmasi.ummc.edu.my/ummc-on-line-antibiotic-guideline. Accessed: 15 January 2022.
- University Kebangsaan Malaysia Medical Centre (2012) PPUKM anti-infective guideline. Available: https://hctm.ukm.my/farmasi/wpcontent/uploads/2020/08/Anti-Infective-Guideline-2012-2MB.pdf. Accessed: 22 January 2022.
- 24. Ministry of Health Malaysia (2014) National antibiotic guideline. Available: https://www.pharmacy.gov.my/v2/sites/default/files/documen t-upload/national-antibiotic-guideline-2014-full-versionjun2015 1.pdf. Accessed: 7 January 2022.
- 25. Atif M, Azeem M, Saqib A, Scahill S (2017) Investigation of antimicrobial use at a tertiary care hospital in Southern Punjab,

Pakistan using WHO methodology. Antimicrob Resist Infect Control 6: 1–12.

- Ansari F, Erntell M, Goossens H, Davey P, Group EIIHCS (2009) The European surveillance of antimicrobial consumption (ESAC) point-prevalence survey of antibacterial use in 20 European hospitals in 2006. Clin Infect Dis 49: 1496– 1504.
- 27. Roberts SC, Zembower TR (2021) Global increases in antibiotic consumption: a concerning trend for WHO targets. Lancet Infect Dis 21: 10–11.
- Jones R, Carville K, James R (2020) Antimicrobial stewardship in Australian hospitals: how does compliance with antimicrobial stewardship standards compare across key hospital classifications? JAC-antimicrobial Resist 2: dlaa100.
- 29. Center for Disease Control and Prevention (2021) Core elements of antibiotic stewardship. Available: https://www.cdc.gov/antibiotic-use/core-elements/index.html. Accessed: 28 January 2022.
- Murray C, Shaw A, Lloyd M, Smith RP, Fardon TC, Schembri S, Chalmers JD (2014) A multidisciplinary intervention to reduce antibiotic duration in lower respiratory tract infections. J Antimicrob Chemother 69: 515–518.
- Leekha S, Terrell CL, Edson RS (2011) General principles of antimicrobial therapy. Mayo Clinic proceedings. Vol. 86. 156– 167.
- 32. Milo G, Katchman E, Paul M, Christiaens T, Baerheim A, Leibovici L (2005) Duration of antibacterial treatment for uncomplicated urinary tract infection in women. Cochrane Database Syst Rev 2: CD004682.
- 33. Dunbar LM, Wunderink RG, Habib MP, Smith LG, Tennenberg AM, Khashab MM, Wiesinger BA, Xiang JX, Zadeikis N, Kahn JB (2003) High-dose, short-course levofloxacin for community-acquired pneumonia: A new treatment paradigm. Clin Infect Dis 37: 752–760.
- 34. Chastre J, Wolff M, Fagon J-Y, Chevret S, Thomas F, Wermert D, Clementi E, Gonzalez J, Jusserand D, Asfar P (2003) Comparison of 8 vs 15 days of antibiotic therapy for ventilatorassociated pneumonia in adults: a randomized trial. Jama 290: 2588–2598.
- 35. Pugh R, Grant C, Cooke RPD, Dempsey G (2011) Short-course versus prolonged-course antibiotic therapy for hospital-acquired pneumonia in critically ill adults. Cochrane Database Syst Rev.
- 36. Al-Mouqdad MM, Aljobair F, Alaklobi FA, Taha MY, Abdelrahim A, Asfour SS (2018) The consequences of prolonged duration of antibiotics in premature infants with suspected sepsis in a large tertiary referral hospital: a retrospective cohort study. Int J Pediatr Adolesc Med 5: 110– 115.
- Hecker MT, Aron DC, Patel NP, Lehmann MK, Donskey CJ (2003) Unnecessary use of antimicrobials in hospitalized patients: current patterns of misuse with an emphasis on the antianaerobic spectrum of activity. Arch Intern Med 163: 972– 978.
- Tamma PD, Avdic E, Li DX, Dzintars K, Cosgrove SE (2017) Association of adverse events with antibiotic use in hospitalized patients. JAMA Intern Med 177: 1308–1315.
- Abdalla SN, Yousef BA (2019) Prescribing patterns of antimicrobials in the internal medicine department of Ibrahim Malik teaching hospital in Khartoum, 2016. Pan Afr Med J 34.
- Al Ashiru-Oredope D, Richards M, Giles J, Smith N, Teare L (2011) Does an antimicrobial section on a drug chart influence prescribing? Clin Pharm. Available: https://pharmaceutical-

journal.com/article/research/does-an-antimicrobial-sectionon-a-drug-chart-influence-prescribing. Accessed: 21 January 2022.

- 41. Yeo JM (2016) Antimicrobial stewardship: improving antibiotic prescribing practice in a respiratory ward. BMJ Open Qual 5: u206491-w3570.
- 42. Timmons V, Townsend J, McKenzie R, Burdalski C, Adams-Sommer V (2018) An evaluation of provider-chosen antibiotic indications as a targeted antimicrobial stewardship intervention. Am J Infect Control 46: 1174–1179.
- 43. Goss FR, Bookman K, Barron M, Bickley D, Landgren B, Kroehl M, Williamson K, Zane R, Wiler J (2020) Improved antibiotic prescribing using indication-based clinical decision support in the emergency department. J Am Coll Emerg Physicians Open 1: 214–221.
- 44. Buising KL, Thursky KA, Robertson MB, Black JF, Street AC, Richards MJ, Brown G V (2008) Electronic antibiotic stewardship—reduced consumption of broad-spectrum antibiotics using a computerized antimicrobial approval system in a hospital setting. J Antimicrob Chemother 62: 608–616.
- 45. Douglas AP, Hall L, James RS, Worth LJ, Slavin MA, Thursky KA (2021) Quality of inpatient antimicrobial use in hematology and oncology patients. Infect Control Hosp Epidemiol 42: 1235–1244.
- 46. World Health Organization (2022) Essential medicines. Available: https://www.who.int/southeastasia/healthtopics/essential-medicines. Accessed: 28 January 2022
- 47. Jesse S, Hawes L, Biezen R, Arjun R (2019) Timely recommendations for addressing overuse of antibiotics.

Available: https://www.croakey.org/timely-recommendationsfor-addressing-overuse-of-antibiotics/. Accessed: 9 January 2022.

- 48. Vandael E, Latour K, Goossens H, Magerman K, Drapier N, Catry B, Versporten A (2020) Point prevalence survey of antimicrobial use and healthcare-associated infections in Belgian acute care hospitals: results of the Global-PPS and ECDC-PPS 2017. Antimicrob Resist Infect Control 9: 1–13.
- 49. Mol PGM, Wieringa JE, NannanPanday P V, Gans ROB, Degener JE, Laseur M, Haaijer-Ruskamp FM (2005) Improving compliance with hospital antibiotic guidelines: A time-series intervention analysis. J Antimicrob Chemother 55: 550–557.
- Rodrigues AT, Roque F, Falcão A, Figueiras A, Herdeiro MT (2013) Understanding physician antibiotic prescribing behaviour: A systematic review of qualitative studies. Int J Antimicrob Agents 41: 203–212.

Corresponding author

Dr Sasheela Ponnampalavanar, Department of Medicine, University Malaya Medical Center Jalan Profesor Diraja Ungku Aziz 59100 Kuala Lumpur, Malaysia. Telephone: +603-7949 4422 Email: sheela@ummc.edu.my

Conflict of interests: No conflict of interests is declared.