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 Jamaluddin2,3, Isa Naina-Mohamed2, Petrick Periyasamy4, Chee Lan Lau2,5, 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 multidrug-resistant 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 real-life multifaceted patient scenarios that require clinical judgment [5]. Process measures of clinical 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
respectively 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.

<table>
<thead>
<tr>
<th>Ranking</th>
<th>Most common specialty</th>
<th>UMMC (n = 178) (%. n)</th>
<th>HCTM (n = 194) (%. n)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>General Medicine# (54.5%, 97)</td>
<td>General Medicine# (61.3%, 119)</td>
<td>0.181</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Haematology (14.6%, 26)</td>
<td>Haematology (22.2%, 43)</td>
<td>0.061</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Cardiology (11.8%, 21)</td>
<td>Cardiology (2.1%, 4)</td>
<td>&lt; 0.001*</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Nephrology (10.1%, 18)</td>
<td>Nephrology (9.3%, 18)</td>
<td>0.786</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Infectious disease (9.0%, 16)</td>
<td>Infectious disease (5.2%, 10)</td>
<td>0.147</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ranking</th>
<th>Most common site of infection</th>
<th>UMMC (n = 178) (%. n)</th>
<th>HCTM (n = 194) (%. n)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Respiratory (28.7%, 51)</td>
<td>Respiratory (36.6%, 71)</td>
<td>0.103</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Sepsis and bacteraemia (14.6%, 26)</td>
<td>Sepsis and bacteraemia (12.4%, 24)</td>
<td>0.528</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Medical prophylaxis (10.7%, 19)</td>
<td>Medical prophylaxis (16%, 31)</td>
<td>0.134</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Other (10.1%, 18)</td>
<td>Other (2.6%, 5)</td>
<td>0.004*</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Systemic infection (7.3%, 13)</td>
<td>Systemic infection (5.7%, 11)</td>
<td>0.522</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Skin and soft tissue infection (7.3%, 13)</td>
<td>Skin and soft tissue infection (6.2%, 12)</td>
<td>0.667</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ranking</th>
<th>Most common antimicrobials prescribed</th>
<th>UMMC (n = 178) (%. n)</th>
<th>HCTM (n = 194) (%. n)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Amoxicillin – clavulanic acid (16.9%, 30)</td>
<td>Amoxicillin – clavulanic acid (11.9%, 23)</td>
<td>0.168</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Piperacillin – tazobactam (12.4%, 22)</td>
<td>Piperacillin – tazobactam (9.8%, 19)</td>
<td>0.430</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Ceftriaxone (5.1%, 9)</td>
<td>Ceftriaxone (10.8%, 21)</td>
<td>0.041*</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Flucloxacillin (5.1%, 9)</td>
<td>Flucloxacillin (3.6%, 7)</td>
<td>0.492</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Cloxacillin (4.5%, 8)</td>
<td>Cloxacillin (3.1%, 6)</td>
<td>0.478</td>
<td></td>
</tr>
</tbody>
</table>

*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 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, Haematology 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 Haematology 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].

Table 2. Appropriateness of antimicrobial prescribing for the three most common specialty, sites of infection and antimicrobials.

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

*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 (ACSQHC) 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>
<thead>
<tr>
<th>Reason</th>
<th>UMMC (n = 135) (%, n)</th>
<th>HCTM (n = 56) (%, n)</th>
<th>$p$ valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergy mismatch</td>
<td>1.5%, 2</td>
<td>3.4%, 2</td>
<td>0.496b</td>
</tr>
<tr>
<td>Microbiology mismatch</td>
<td>2.2%, 3</td>
<td>1.7%, 1</td>
<td>0.615b</td>
</tr>
<tr>
<td>Incorrect route</td>
<td>6.7%, 9</td>
<td>5.2%, 3</td>
<td>0.317b</td>
</tr>
<tr>
<td>Incorrect dose and/or frequency</td>
<td>23.7%, 32</td>
<td>24.1%, 14</td>
<td>0.342</td>
</tr>
<tr>
<td>Incorrect duration</td>
<td>14.8%, 20</td>
<td>25.9%, 15</td>
<td>0.017*</td>
</tr>
<tr>
<td>Spectrum too broad</td>
<td>20.0%, 27</td>
<td>20.7%, 12</td>
<td>0.444</td>
</tr>
<tr>
<td>Spectrum too narrow</td>
<td>25.2%, 34</td>
<td>20.7%, 12</td>
<td>0.030*</td>
</tr>
<tr>
<td>Antimicrobials not indicated</td>
<td>11.1%, 15</td>
<td>22.4%, 13</td>
<td>0.003*</td>
</tr>
</tbody>
</table>

*aStatistically significant at $p < 0.05$; *bChi-Squared, *cFisher 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], community-acquired pneumonia for five days [33], and ventilator-associated 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 amoxicillin-clavulanic 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-and-answer 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 duration, dosage, indication, 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

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 Ponnamapalanavan, 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


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.