Antibiotic Prescribing for Upper Respiratory Tract Infections in Sarawak District Hospitals

Boon Phiaw Kho, BPharm*, Charlene Mei Yian Ong, MPharm**, Freda Tze Yin Tan, BPharm***, Chee Yang Wee, BPharm***

SUMMARY
Upper respiratory tract infection (URTI) is mostly viral in aetiology, but patients presenting with such complaints are frequently prescribed antibiotics. This may result in increased development of antimicrobial resistance. The objectives of this study are to determine the choice and proportion of oral antibiotics prescribed in patients with URTI, in a Sarawak district hospital setting. All outpatient prescriptions received in July 2011 in 10 hospitals with relevant diagnoses were analysed. A total of 6747 URTI prescriptions met the inclusion criteria, and 64.8% (95% CI 63.7%, 65.9%) had antibiotic prescribed. Medical Assistants (MAs) were significantly more likely to prescribe antibiotics compared to Medical Officers (MOs) (p < 0.001). Prescribers were significantly influenced by the patient’s age and specific diagnosis when prescribing antibiotics for URTI (p < 0.001). Antibiotic choices differed between MOs and MAs, where some of the antibiotic choices were inappropriate. There is a need for multi-faceted interventions to improve antibiotic prescribing rate and choice.

KEY WORDS:
Upper respiratory tract infection, antibiotics, district hospital, prescribing

INTRODUCTION
Upper respiratory tract infection (URTI) is a ubiquitous infection that results in numerous visits to primary care facilities. In the United States, it accounts for over 37 million visits in a single year. In Malaysia, it was found to contribute to approximately 30% of visits to private and government healthcare clinics. URTI is an umbrella term which encompasses sinus, pharyngeal and lower airway symptoms, where none of the symptoms are dominant and the exact site of infection cannot be clearly established.

URTI is primarily viral in aetiology and in most cases, will resolve spontaneously within one to two weeks. The main bacterial pathogen in URTI is the group A β-haemolytic streptococcus (GBHS), which was found to be present in only 2.4 to 17% of adults who presented with URTI symptoms. Despite this, the usage of antibiotics to treat this condition was noted to be inappropriately high on a worldwide scale. In India, 69.4% of patients with uncomplicated acute respiratory infections were prescribed antibiotics. Antibiotic overprescribing is also evident in children, with 74% of children with URTI in the United States receiving antibiotic prescriptions. In a Malaysian setting, the most recent study found antibiotic prescribing for URTI in primary healthcare clinics (public and private) to be 33.8%.

The non-judicious use of antibiotics for the treatment of URTI is not recommended as antibiotics are ineffective in resolving infections of a viral aetiology. A retrospective cohort study in the United Kingdom concluded that the complication rate after URTI is very low, and antibiotic therapy to prevent complications after URTI is not effective, as a number needed to treat (NNT) of over 4000 is needed to prevent an episode of pneumonia. Conversely, the inappropriate prescribing of antibiotics in viral infections has resulted in an increasing growth rate of antibiotic resistance worldwide. Even short-term use of antibiotics can create increased antimicrobial resistance for up to 3 months. There is evidence of a marked increase in the number of antibiotic-resistant bacteria, including Streptococcus pneumoniae, a leading causative agent of community acquired pneumonia.

Sarawak is by far the largest state in Malaysia, scattered with 22 government hospitals, of which 16 (Bau, Betong, Dalat, Daro, Kanowit, Kapit, Lundu, Lawas, Limbang, Marudi, Mukah, Saratok, Sarikie, Serian, Simunjan, Sari Aman) are considered district hospitals, serving rural communities. The clinics and emergency and trauma units in these district hospitals are run by Medical Officers (MOs) and Medical Assistants (MAs). MAs play an integral role in the screening and provision of medical treatment to patients, including prescribing for minor ailments in district hospitals due to a shortage of MOs. Although a study on the rate of antibiotic prescribing in primary care clinics in Malaysia was recently carried out, we have found no literature regarding the rate of antibiotic prescriptions in a district hospital setting in Malaysia, specifically in the state of Sarawak.

The main objectives of this study are to determine the choice and proportion of oral antibiotics prescribed in patients diagnosed with URTI, in a Sarawak district hospital setting. The influence of the patient’s age, the specific diagnosis and the type of prescriber (MO or MA) on the antibiotic prescribing rates were also determined.

MATERIALS AND METHODS
Data collection:
This was a retrospective study carried out in 10 district hospitals, of which 10 (Bau, Betong, Dalat, Daro, Kanowit, Kapit, Lundu, Lawas, Limbang, Marudi, Mukah, Saratok, Sarikie, Serian, Simunjan, Sari Aman) are considered district hospitals, serving rural communities. The clinics and emergency and trauma units in these district hospitals are run by Medical Officers (MOs) and Medical Assistants (MAs). MAs play an integral role in the screening and provision of medical treatment to patients, including prescribing for minor ailments in district hospitals due to a shortage of MOs. Although a study on the rate of antibiotic prescribing in primary care clinics in Malaysia was recently carried out, we have found no literature regarding the rate of antibiotic prescriptions in a district hospital setting in Malaysia, specifically in the state of Sarawak.

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hospitals in Sarawak. The hospitals involved in this study were Bau Hospital, Betong Hospital, Kanowit Hospital, Lawas Hospital, Limbang Hospital, Mukah Hospital, Saratok Hospital, Serian Hospital, Simunjan Hospital and Sri Aman Hospital. All outpatient prescriptions received from the 1st to the 31st of July 2011 were analysed. All outpatient prescriptions with the diagnosis of ‘URTI’, ‘tonsillitis’, ‘pharyngitis’, ‘common cold’, ‘sore throat’ or ‘otitis media’ were included in the study. Outpatient prescriptions where the age or diagnosis of the patient was not documented, or having a diagnosis of more than 1 infection were excluded from this study. The following information was recorded: prescription date and number, age of patient (in age groups), diagnosis, prescriber (MO or MA) and if an oral antibiotic was prescribed, the name, dose and duration of the antibiotic.

Statistical analysis:
Data were entered into a Microsoft Excel Spreadsheet and exported for analyses using the Statistical Package for Social Sciences (SPSS, version 18.0). Chi-square test was used to investigate the differences in antibiotic prescriptions by age groups, prescribers and specific diagnosis. Statistical significance was set to be p < 0.05.

RESULTS
A total of 6747 prescriptions collected from 10 district hospital pharmacies in Sarawak matched the inclusion criteria specified and were included for analysis. The proportion of prescriptions for URTI with antibiotics prescribed was 64.8% (95% CI 63.7%, 65.9%).

Approximately half the patients (56.3%) presenting with URTI symptoms were below 20 years of age. From Table I, it can be seen that the age of the patient influenced the prescription of antibiotics (p < 0.001). Further analysis indicated that those aged below 20 years were more likely to be prescribed antibiotics compared to patients above 21 years (68.7% vs 59.8%, X² = 58.01; p < 0.001).

A very small proportion of patients (6.2%) with URTI were seen by MOs. Table I shows that MAs were significantly more likely to prescribe antibiotics for URTI compared to MOs (p < 0.001). About half the patients (48.9%) with URTI were prescribed antibiotics after MO consultation, compared to 65.8% of patients who were prescribed antibiotics after presenting to MAs with URTI symptoms.

Prescribers were more likely to prescribe antibiotics for patients diagnosed with tonsillitis and pharyngitis (97.0% and 95.0% respectively), as depicted in Table I. For patients

Table I: Factors influencing antibiotic prescribing for URTI (n = 6747)

<table>
<thead>
<tr>
<th>Age bracket (years)</th>
<th>n With antibiotics n (%)</th>
<th>Without antibiotics n (%)</th>
<th>X² statistic (df)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2</td>
<td>981</td>
<td>635 (64.7)</td>
<td>346 (35.3)</td>
<td>78.44 (5)</td>
</tr>
<tr>
<td>3-12</td>
<td>2011</td>
<td>1394 (69.3)</td>
<td>617 (30.7)</td>
<td></td>
</tr>
<tr>
<td>13-20</td>
<td>804</td>
<td>579 (72.0)</td>
<td>225 (28.0)</td>
<td></td>
</tr>
<tr>
<td>21-40</td>
<td>1141</td>
<td>697 (61.1)</td>
<td>444 (38.9)</td>
<td></td>
</tr>
<tr>
<td>41-60</td>
<td>1263</td>
<td>771 (61.0)</td>
<td>492 (39.0)</td>
<td></td>
</tr>
<tr>
<td>≥ 61</td>
<td>547</td>
<td>296 (54.1)</td>
<td>251 (45.9)</td>
<td></td>
</tr>
</tbody>
</table>

Prescriber

| MO                  | 417                     | 204 (48.9)                | 213 (51.1)       | 49.13 (1) | <0.001 |
| MA                  | 6330                    | 4168 (65.8)               | 2162 (34.2)      |          |       |

Specific diagnosis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n With antibiotics n (%)</th>
<th>Without antibiotics n (%)</th>
<th>X² statistic (df)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>URTI</td>
<td>5793</td>
<td>3553 (61.3)</td>
<td>2240 (38.7)</td>
<td>508.43 (5)</td>
</tr>
<tr>
<td>Tonsillitis</td>
<td>656</td>
<td>636 (97.0)</td>
<td>20 (3.0)</td>
<td></td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>120</td>
<td>114 (95.0)</td>
<td>6 (5.0)</td>
<td></td>
</tr>
<tr>
<td>Common cold</td>
<td>76</td>
<td>3 (3.9)</td>
<td>73 (96.1)</td>
<td></td>
</tr>
<tr>
<td>Sore Throat</td>
<td>27</td>
<td>11 (40.7)</td>
<td>16 (59.3)</td>
<td></td>
</tr>
<tr>
<td>Otitis Media</td>
<td>75</td>
<td>55 (73.3)</td>
<td>20 (26.7)</td>
<td></td>
</tr>
</tbody>
</table>

a Chi-square test for independence

Table II: Choice of antibiotics prescribed for URTI according to prescriber

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Prescribed by MO n (%)</th>
<th>Prescribed by MA n (%)</th>
<th>Total n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacampicillin</td>
<td>35 (17.1)</td>
<td>1544 (37.0)</td>
<td>1579 (36.1)</td>
</tr>
<tr>
<td>Phenoxymethylpenicillin</td>
<td>9 (4.4)</td>
<td>837 (20.1)</td>
<td>846 (19.4)</td>
</tr>
<tr>
<td>Erythromycin ethylsuccinate</td>
<td>35 (17.2)</td>
<td>783 (18.8)</td>
<td>818 (18.7)</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>26 (12.7)</td>
<td>668 (16.0)</td>
<td>694 (15.9)</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>83 (40.7)</td>
<td>289 (6.9)</td>
<td>372 (8.5)</td>
</tr>
<tr>
<td>Cloxacillin</td>
<td>1 (0.5)</td>
<td>44 (1.1)</td>
<td>45 (1.0)</td>
</tr>
<tr>
<td>Amoxicillin/clavulanic acid</td>
<td>7 (3.4)</td>
<td>0 (0.0)</td>
<td>7 (0.2)</td>
</tr>
<tr>
<td>Erythromycin stearate</td>
<td>0 (0.0)</td>
<td>3 (0.1)</td>
<td>3 (0.1)</td>
</tr>
<tr>
<td>Erythromycin ethylsuccinate + amoxicillin</td>
<td>3 (1.5)</td>
<td>0 (0.0)</td>
<td>3 (0.1)</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>2 (1.0)</td>
<td>0 (0.0)</td>
<td>2 (&lt;0.1)</td>
</tr>
<tr>
<td>Co-trimoxazole</td>
<td>1 (0.5)</td>
<td>0 (0.0)</td>
<td>1 (&lt;0.1)</td>
</tr>
<tr>
<td>Erythromycin ethylsuccinate + cloxacillin</td>
<td>1 (0.5)</td>
<td>0 (0.0)</td>
<td>1 (&lt;0.1)</td>
</tr>
<tr>
<td>Amoxicillin + cloxacillin</td>
<td>1 (0.5)</td>
<td>0 (0.0)</td>
<td>1 (&lt;0.1)</td>
</tr>
</tbody>
</table>
diagnosed with URTI, 61.3% were prescribed with antibiotics. Only 3.9% of patients presenting with the common cold were prescribed with antibiotics. The specific diagnosis of URTI was shown to significantly influence antibiotic prescribing (p < 0.001).

The choice of antibiotics prescribed for URTI is depicted in Table II. Overall, bacampicillin was the most commonly prescribed antibiotic (36.1%). The top choices of antibiotics for URTI varied between MOs and MAs. The most frequently prescribed antibiotic for URTI among MOs was amoxycillin (40.7%), while that among the MAs was bacampicillin (37.0%). There were five prescriptions (0.1%) containing a combination of two antibiotics for URTI. All five prescriptions were written by MOs.

DISCUSSION

The antibiotic prescribing rate of 64.8% for URTI in Sarawak district hospitals is very high and should be a cause for concern. This rate is much higher than the reported figures of 27.7% and 27.8% of patients with URTI being given antibiotics in Malaysian public primary care facilities. There are cases that warrant treatment of URTI with antibiotics, for example, where the patient has at least 3 of these symptoms: presence of tonsillar exudate, tender cervical lymphadenopathy or lymphadenitis, history of fever and absence of cough; but in most cases, antibiotic prescribing is unjustified as URTI is mainly viral in aetiology. This indicates that most prescribers are still not well-aware of the concept and implications of antibiotic resistance. Therefore, they do not take these into consideration when they decide whether or not to prescribe antibiotics for URTI.

Previous studies have shown a variety of results regarding the influence of age on antibiotic prescribing. In the United States, antibiotics were prescribed more often to children aged 5 – 11 years than younger children of below 5 years. In another study in India, antibiotics were more frequently prescribed for URTI in children aged between 6 and 18 years compared to adults. However, in a Malaysian study, Teng et al. (2011) found no difference between the antibiotic prescribing rates for children and adults. The results from this study concur with the findings of Kumari Indira et al. (2008), with children and adolescents more likely to be prescribed with antibiotics compared to adults. This may be due to pressure from accompanying parents, as a local study by Chan and Tang (2006) reported that nearly 30% of parents requested for their children to be given antibiotics for URTI symptoms. Prescribers may also feel that children and teenagers have a higher risk of post URTI complications. However, this prescribing pattern is not justified, as the study by Peterson et al. (2007) indicated that older patients have a higher risk of developing pneumonia post one month after diagnosis of URTI compared to their younger counterparts.

The antibiotic prescribing rate of MAs in this study was found to be significantly higher compared to MOs. In contrast, there was no significant difference between the antibiotic prescribing rate of MOs and MAs from government clinics in the Seremban district. This difference could be contributed to the Hawthorne effect, which was likely to be present in the study by Teng et al. (2003) as the prescribers were aware of the study being carried out, unlike in the current study. Better knowledge on antibiotic usage and appreciation of antibiotic resistance of MOs may account for the significant difference found in this study.

This study showed that prescribers based antibiotic prescribing on the specific diagnosis of the patient. Antibiotics were prescribed in nearly all cases of tonsillitis and pharyngitis, which meant that they believed that most of these cases were of bacterial aetiology. However, the very low rate of antibiotic prescribing for the common cold meant that prescribers were confident that the common cold was not caused by bacterial infection and seldom warranted treatment with antibiotics. This was interesting as the specific diagnosis should not have been a determinant for antibiotic prescribing in URTI.

Phenoxyymethylpenicillin and erythromycin, the recommended antibiotics for URTI, made up nearly 40% of URTI prescriptions with antibiotics in this study. The prescribers, especially the MOs, highly favoured the broad-spectrum penicillins such as amoxycillin, ampicillin and bacampicillin. Although these broad-spectrum antibiotics are generally as effective as phenoxyymethylpenicillin against GABHS, previous research have shown that wide-spread use of amoxycillin and bacampicillin have resulted in high rates of antibiotic resistance.

The choice of antibiotics prescribed in this study was limited to the Ministry of Health Drug Formulary (2009). A larger variation of antibiotics was prescribed by the MOs because they have the authority to prescribe a wider range of antibiotics compared with the MAs. Under the Ministry of Health Drug Formulary (2009), phenoxyymethylpenicillin is the only antibiotic which can be prescribed by MAs. However, as a large proportion of the patients presenting with URTI in district hospitals are screened and treated by MAs, most district hospital policies allow MAs to prescribe a few other antibiotics, including bacampicillin, amoxycillin and erythromycin. The low prescribing rate of amoxycillin/clavulanic acid and ceftroxime can be explained by the fact that these antibiotics require approval by a medical specialist, as specified in the Ministry of Health Drug Formulary (2009). The results may also indicate that prescribers choose antibiotics based on the ease of dosing. Bacampicillin and erythromycin ethylsuccinate, which made up 54.5% of total antibiotics prescribed, are both twice daily dosing.

It was interesting to note some of the inappropriate management of URTI, such as the prescribing of cloxacillin and co-trimoxazole, which are not sensitive against GABHS. There is also no indication for the use of two antibiotics to treat URTI. However, as the diagnosis of the patient was based solely on the diagnosis on the prescription, there is a possibility that the MOs were treating another bacterial infection not documented on the prescription.

Multi-faceted interventions are necessary to improve the prescribing rate of antibiotics. These strategies include interactive educational meetings, physician reminders,
patient education and the use of delayed prescriptions\textsuperscript{22}. Educational intervention, consisting of academic detailing and information leaflets has successfully reduced antibiotic prescribing in a Malaysian public primary care clinic setting\textsuperscript{3}. Another possible educational intervention would be strengthening the curriculum on appropriate antibiotic prescribing for MA trainees and medical students during their years in college or university.

Delayed antibiotic prescriptions may effectively reduce antibiotic use by patients\textsuperscript{23}. Patients with acute otitis media, acute sore throat/acute pharyngitis/acute tonsillitis, common cold, acute rhinosinusitis or acute cough/acute bronchitis where antibiotics are not needed immediately may be given a delayed prescription, which is to be used if symptoms do not settle or significantly worsen\textsuperscript{24}. Although this method holds merit, it may not be practical in the Sarawak district setting because of logistic issues. Transportation is often a problem for patients from rural villages, who rely on hiring vehicles to get to the hospital, which could be costly and may take one to two hours for a one-way journey. However, this could be successfully implemented for patients with no transportation issues and/or are staying nearer to the hospital.

Prescribers play an important role in explaining to patients that the infection is self-limiting, and that antibiotics are not only ineffective in viral infections, but may also result in adverse effects such as gastrointestinal upset\textsuperscript{25}. Patients strongly influence antibiotic prescribing by directly requesting for antibiotics, suggesting or implying diagnosis, giving an impression of the severity of the illness, or volunteering past successful experiences with antibiotics\textsuperscript{26}. In a study in Singapore, only 7.9\% of patients knew that URTI is a viral disease, and only 36.3\% of patients were aware of URTI being self-limiting\textsuperscript{27}. A study by Oh et al. (2011)\textsuperscript{28} carried out in Penang, Malaysia revealed that only 16\% of the public had a good level of knowledge on antibiotics; with the knowledge level positively correlating with education level and income. As patients in rural areas generally have lower income and education level, it is even more pertinent to emphasize on patient education here. Educating patients that most cases of URTI will resolve on its own and on the correct usage of antibiotics may improve patients’ health-seeking behaviour.

\textbf{STUDY LIMITATIONS}

This study depends on the prescriber writing the correct diagnosis on the prescription. Some patients may have presented with URTI, but this was not documented on the prescription by the prescriber. The classification of URTI by the MOs and MAs involved may have varied according to their own interpretations and experiences. The proportion of patients seen by MOs was very small, as URTI is generally viewed as a minor ailment, and so these patients are rarely referred by the MAs to the MOs. Therefore the antibiotic prescribing rate and choices of the MOs might not be generalised to all MOs in a public district hospital setting.

Only URTI prescriptions with oral antibiotics were included, therefore, there might be an under-estimation of the antibiotics prescribed in otitis media as antibacterial eardrops such as chloramphenicol eardrops are commonly prescribed for this ailment. As this study relied on the diagnosis written on the prescription and not the microbiological culture and clinical presentation of the patient, we were unable to comment on the appropriateness of the antibiotic prescription. Lastly, no temporal relationship can be established in this study as the study design cannot capture the outcome of the patient involved.

\textbf{CONCLUSION}

This study showed that there was an inappropriately high rate of antibiotic prescribing for URTI in Sarawak district hospitals. Antibiotic prescribing for URTI was influenced by the patient’s age, the specific diagnosis and whether the prescriber is a MO or MA. Antibiotic choices varied between MOs and MAs, where some of the antibiotic choices were inappropriate due to insensitivity to GABHS. There is a need for further studies to elucidate the causes and motivation for this high prescription rate as well as institution of multifaceted interventions to improve antibiotic prescribing rate and choice.

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\textbf{REFERENCES}


