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Appropriateness of antibiotic prescribing in the Emergency Department

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Background: Antibiotics are some of the most commonly prescribed drugs in the Emergency Department (ED) and yet data describing the overall appropriateness of antibiotic prescribing in the ED is scarce.

Objectives: To describe the appropriateness of antibiotic prescribing in the ED.

Methods: A retrospective, observational study of current practice. All patients who presented to the ED during the study period and were prescribed at least one antibiotic were included. Specialists from Infectious Disease, Microbiology and Emergency Medicine and a Senior Pharmacist assessed antibiotic appropriateness against evidence-based guidelines.

Results: A total of 1019 (13.6%) of patient presentations involved the prescription of at least one antibiotic. Of these, 640 (62.8%) antibiotic prescriptions were assessed as appropriate, 333 (32.7%) were assessed as inappropriate and 46 (4.5%) were deemed to be not assessable. Adults were more likely to receive an inappropriate antibiotic prescription than children (36.9% versus 22.9%; difference 14.1%, 95% CI 7.2%–21.0%). Patients who met quick Sepsis-related Organ Failure Assessment (qSOFA) criteria were more likely to be prescribed inappropriate antibiotics (56.7% versus 36.1%; difference 20.5%, 95% CI, 2.4%–38.7%). There was no difference in the incidence of appropriate antibiotic prescribing based on patient gender, disposition (admitted/discharged), reason for antibiotic administration (treatment/prophylaxis) or time of shift (day/night).

Conclusions: Inappropriate administration of antibiotics can lead to unnecessary adverse events, treatment failure and antimicrobial resistance. With over one in three antibiotic prescriptions in the ED being assessed as inappropriate, there is a pressing need to develop initiatives to improve antibiotic prescribing to prevent antibiotic-associated patient and community harms.

Introduction

The timely administration of appropriate antibiotics in the Emergency Department (ED) can be lifesaving.[1] However, antibiotics are not a benign intervention and unnecessary or inappropriate antibiotics can lead to patient and community harms, including the harms associated with adverse events, treatment failure and antimicrobial resistance (AMR).[2,3] A recent study by Tamma *et al.*[2] found that among patients to whom antibiotics were administered in hospital, one in five experienced a clinically significant antibiotic-associated adverse drug event.

The ED is an important setting for addressing inappropriate antibiotic prescribing practices, given that it sits at the interface of the community and the hospital.[4] The ED is also unique in its challenges to appropriate antibiotic prescribing, with ED-based clinicians frequently faced with the combination of both diagnostic uncertainty and time pressure.[5] However, despite this, antimicrobial stewardship (AMS) initiatives are rarely tailored to the ED[6] and data describing the overall incidence of inappropriate prescribing in the ED to inspire such initiatives are scarce.

We therefore aimed to describe the overall incidence of antibiotic prescribing in a busy, tertiary-level academic ED. Further, the

appropriateness of antibiotic prescriptions was judged against evidence-based guidelines or, in cases in which endorsed guidelines were not available or applicable, by expert opinion using a previously validated antibiotic appropriateness assessment tool. We additionally assessed antibiotic appropriateness for predefined subgroups based on age, gender, indication for antibiotics (treatment versus prophylaxis) and whether the patient met the criteria for sepsis.

Patients and methods

Design, setting and population

The study was conducted at a large, public tertiary ED in Queensland, Australia with on-site microbiology and infectious disease specialists. The census in 2016 was 102 286 ED attendances, of which 24.4% were paediatric. The institutional Human Research Ethics Committee approved the study (HREC/17/QGC/41), including a waiver for informed consent owing to the observational nature of the study. Findings are reported in accordance with the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) Statement for cohort studies.[7]

All consecutive patients who presented to the ED over a total period of 4 weeks throughout 2016 (1–7 February; 9–15 May; 22–28 August; 14–20 November) were included. These four weeks were selected prior to data extraction to avoid potential time-of-year-dependent confounders, including seasonal variation and holiday periods.

Data collection

Clinical information of all patients who presented to the ED during the designated study period was reviewed. The electronic Emergency Department Information System was used to identify patients who presented to the ED during the study period. The electronic medical record (EMR) was then reviewed for all patients. For those patients who had an antibiotic prescribed either in the ED or on discharge from the ED, data were extracted from both the EMR and the laboratory information system, AUSLAB, and entered into a pre-formatted database.

Data included patient demographics, comorbidities, indication for antibiotics, type/dose/route of antibiotic(s) prescribed, clinical observations and results of blood tests and cultures. Additional information was collected regarding: patient disposition (discharge home, ED admission, hospital ward admission, ICU admission or death in the ED); hospital length-of-stay; whether infectious disease or microbiology expert advice was sought whilst the patient was in the ED; whether the patient had antibiotics in the 24 h prior to their ED visit; time of antibiotic administration (day shift: 07:30–23:29; night shift: 23:30–07:29); or any known allergy to an antibiotic. If a reason for deviation from antibiotic prescribing guidelines was given (e.g. prior culture and susceptibility results, significant wound contamination) this was also noted. Patients receiving topical antibiotic, antifungal or antiviral medication only were excluded. Four patients were prescribed antiviral medication only during the study period.

The presumed indication for antibiotic prescribing was taken from the treating clinician's working diagnosis as documented in the medical record. Indications were then grouped into two main categories: (i) treatment of presumed infection; or (ii) prophylaxis. Treatment of presumed infection was then further categorized based on the site of presumed infection: abdominal (e.g. diverticulitis, appendicitis); CNS (e.g. meningitis); dental (e.g. dental abscess); ear/nose/throat (e.g. otitis media, tonsillitis); gynaecological (e.g. pelvic inflammatory disease); orthopaedic (e.g. osteomyelitis); respiratory (e.g. pneumonia); skin (e.g. cellulitis, skin abscess); urinary (e.g. cystitis, pyelonephritis); unknown source; or other (i.e. not fitting into aforementioned categories). Prophylaxis was further categorized into: bite prophylaxis; surgical prophylaxis; wound prophylaxis; or other (i.e. not fitting into aforementioned categories). When the medical record was incomplete or unavailable or the indication for antibiotics was unclear, the label of 'unknown indication' was applied.

Derived variables included Systemic Inflammatory Response Syndrome (SIRS) and quick Sepsis-related Organ Failure Assessment (qSOFA) scores. These scores have been proposed as tools to assist in the identification of patients with infection and identification of those who are at a greater risk of a poor outcome, respectively.[8,9] Patients over the age of 18 years met SIRS criteria if they had two or more of: temperature $\geq$38°C or <36°C; heart rate >90 beats/min; respiratory rate >20 breaths/min; or white blood cell count $>12\times10^9$/L or $<4\times10^9$/L. Patients over the age of 18 years met qSOFA criteria if they had two or more of: Glasgow Coma Scale <15; respiratory rate >22 breaths/min; or systolic blood pressure <100 mmHg. Missing data were handled by assuming the patient did not meet the criteria. There is no current qSOFA equivalent in paediatrics and the use of SIRS criteria in the paediatric population is not based on evidence related to clinical outcomes.[10] The paediatric subpopulation was therefore excluded from calculations of these derived variables.

Assessment of antibiotic appropriateness

Antibiotic appropriateness was assessed by a panel of four experts from the fields of Emergency Medicine, Infectious Disease, Microbiology and a Senior AMS Pharmacist. The experts utilized evidence-based guidelines together with a pre-established antibiotic appropriateness assessment tool, the National Antibiotic Prescribing Survey (NAPS) table (see Table S1, available as Supplementary data at *JAC* Online).[11,12] This tool has been developed using published methods,[13] in which a high rate of inter-rater reliability and high validity was achieved between assessors of varying experience with antimicrobial prescribing. The validity of this approach has been further demonstrated by the consistency of findings from nationwide hospital point-prevalence studies.[14] Notably, each expert was given only data that would have been available to the ED-based prescriber at the time of antibiotic decision-making (i.e. no culture/susceptibility results were provided).

All patient presentations wherein at least one antibiotic was prescribed were randomized and each assigned to two experts. Each expert then independently assessed the antibiotic prescription as being optimal (1), adequate (2), suboptimal (3), inadequate (4) or not assessable (5) as per NAPS guidelines.[12] If there was no agreement between the two expert assessors—wherein disagreement was defined as two assessors assigning a different score, except when assessors scored a (1) and a (2)—then the case was discussed between all four experts at a round-table discussion. Seven cases required round-table discussion. If an antibiotic regimen was discussed with an infectious disease or microbiology team at the time of prescribing, an assessment of optimal (1) was automatically given. Reasons for an assessment of inappropriate (3 or 4) were also recorded.

Data analysis and sample size

To determine proportions (including appropriateness of prescription) with a 95% certainty and a two-sided error of 1.8% we calculated that we required a total of 1333 patients who were prescribed antibiotics. Based on an expected prescription rate of 16.5% we required 7500 patients, which equated to 4 weeks of patient presentations. IBM SPSS v24 and Open Source Epidemiologic Statistics for Public Health v3.01 (OpenEpi) were employed to perform descriptive and inferential statistics. For the majority of analyses, NAPS scores were grouped as either appropriate (i.e. NAPS score of 1 or 2) or inappropriate (i.e. NAPS score of 3 or 4). Patient presentations that were assessed as not assessable (5) were excluded. Relationships between categorical variables were assessed using a χ^2 test or Fisher's exact test (where appropriate). The Wilson score interval method was used to calculate 95% CI for proportions, corrected for population size. ORs comparing factors associated with appropriate versus inappropriate prescribing were calculated using the mid-*P* exact conditional maximum likelihood estimate of the OR.

Table 1. Characteristics of patients to whom antibiotics were prescribed in the ED

Patient characteristics	
Total number of patient presentations seen in ED during study period	7497
Total patient presentations involving antibiotics, *n* (%)	1019 (13.6)
Total number of antibiotics prescribed	1670
Age, years, mean (SD)	41.3 (±25.4)
Gender, *n* (%)	
male	527 (51.7)
female	492 (48.3)
Antibiotics <24 h prior to ED presentation, *n* (%)	
yes	201 (19.7)
no	818 (80.3)
Documented antibiotic ADR, *n* (%)	
yes	126 (12.4)
no	893 (87.6)
Disposition, *n* (%)	
discharged home from ED	324 (31.8)
ED short-stay unit	204 (20.0)
admitted to hospital ward	472 (46.3)
operating theatre	9 (0.9)
admitted to ICU	10 (1.0)
Patients prescribed antibiotic(s), *n* (%)	
in the ED ± discharge script	778 (76.3)
on discharge script only	241 (23.7)
Discussed with infectious disease or microbiology team, *n* (%)	
yes	5 (0.5)
no	1014 (99.5)
SIRS criteria met[a]? *n/N* (%)	
yes	200/678 (29.5)
no	478/678 (70.5)
qSOFA criteria met[a]? *n/N* (%)	
yes	32/678 (4.7)
no	646/678 (95.3)

ADR, adverse drug reaction.
[a]SIRS and qSOFA criteria were only applied to patients over the age of 18 years who were prescribed antibiotics to treat presumed infection.

Results

During the study period, a total of 7497 patients presented to the ED. One thousand and nineteen (13.6%; 95% CI 12.8%–14.4%) patients were prescribed at least one antibiotic. Only five (0.5%) patients were discussed with an on-call infectious disease or microbiology clinician. Of patients over 18 years who were prescribed antibiotics for treatment of presumed infection—i.e. excluding those under 18 years of age and those who were prescribed antibiotics for prophylaxis—29.5% (200/678) met SIRS criteria and 4.7% (32/678) met qSOFA criteria for sepsis. Characteristics of patients who were prescribed antibiotics are described in Table 1.

The majority ($n = 843$; 82.7%) of presentations involving an antibiotic prescription were administered with the intention of treating infection and 171 (16.7%) were administered for prophylaxis. For five patients (0.5%) the indication for antibiotics was unclear from the clinician notes. Infections of the skin (20.5%) were the most common indication for prescribing antibiotics, followed by respiratory tract infections (15.7%), urinary tract infections (15.6%) and antibiotic prophylaxis for wounds (11.6%). Of antibiotics administered in the ED, 74.0% were given intravenously, 25.5% were given via the oral route and 0.5% were given intramuscularly. Types of antibiotics prescribed are also detailed (see Table S2).

Of the 1019 patient presentations for which at least one antibiotic was prescribed, 640 (62.8%) were assessed to be optimal or adequate, 152 (14.9%) were assessed to be suboptimal, 181 (17.8%) were assessed to be inadequate and 46 (4.5%) were deemed to be not assessable. Thus, when categorized as a binomial of either appropriate (i.e. optimal or adequate) or inappropriate (suboptimal or inadequate), 65.8% (640/973) were assessed as appropriate (95% CI 62.8%–68.7%) and 34.2% (333/973) were assessed as inappropriate (95% CI 31.3%–37.3%). The most common reason given for an assessment of suboptimal was the antibiotic regimen was too broad and/or there was unnecessary overlap of spectrum (67.8%; 103/152). The most common reason given for an assessment of inadequate was that antibiotics were not required at all (53.6%; 97/181) for the indication provided.

Paediatric patients were more likely to have been prescribed an appropriate antibiotic than adult patients (77.1% versus 63.1%; difference 14.1%; 95% CI 7.2%–21.0%). Of the 678 adult patients eligible for calculation of SIRS and qSOFA scores, 650 (95.9%) were able to be assessed for antibiotic appropriateness. Patients who met qSOFA criteria for sepsis were less likely to be prescribed an appropriate antibiotic than patients who did not (43.3% versus 63.9%; difference 20.5%; 95% CI 2.4%–38.7%). There were no significant differences in the incidence of appropriate antibiotic prescribing between patients who did and did not meet SIRS criteria (68.4% versus 61.5%; difference 6.9%; 95% CI −1.0% to 14.8%) or patients prescribed antibiotics for treatment of presumed infection and those prescribed antibiotics for prophylaxis (66.6% versus 61.5%; difference 5.1%; 95% CI −3.1% to 13.3%). Further, there were no significant differences in the incidence of appropriate prescribing based on gender, patient disposition, triage category or time of shift (day/night). Table 2 describes characteristics of patients prescribed both appropriate and inappropriate antibiotics. Table 3 details the site and assessment of appropriateness for both treatment and prophylactic antibiotic regimens.

Discussion

This study provides important insights into the current practice of antibiotic prescribing in the ED. Our data are unique in that they examine the characteristics of all consecutive patients who were prescribed an antibiotic, rather than limiting data collection to a specific disease condition. This has several benefits, including the overall identification of how frequently antibiotics are prescribed in the ED and the most common conditions for which antibiotics are prescribed; it additionally enables an overall assessment of the appropriateness of ED-based antibiotic prescribing.

The appropriateness of antibiotic prescriptions was judged only on the presumed diagnosis from the EMR and clinical observations/investigations available to the doctor at the time of prescribing in the ED. This method allowed for a practical, 'real-world'

Table 2. Patient/prescription characteristics and appropriateness

Characteristic	Appropriate, *n/N* (%)	Inappropriate, *n/N* (%)	Percentage difference for inappropriate prescribing (95% CI)
Age, years			
<18	145/188 (77.1)	43/188 (22.9)	**14.1% (7.2–21.0)**
≥18	495/785 (63.1)	290/785 (36.9)	
Gender			
female	316/474 (66.7)	158/474 (33.3)	1.7% (−4.2–7.7)
male	324/499 (64.9)	175/499 (35.1)	
Patient disposition			
discharged	203/306 (66.3)	103/306 (33.7)	0.8% (−5.6–7.2)
admitted	437/667 (65.5)	230/667 (34.5)	
Triage category			
1	23/42 (54.8)	19/42 (45.2)	11.2% (−5.3–27.7)
2	108/167 (64.7)	59/167 (35.3)	1.3% (−8.6–11.2)
3	385/576 (66.8)	191/576 (33.2)	0.9% (−6.9–8.7)
4/5	124/188 (66.0)	64/188 (34.0)	(reference)
SIRS criteria met[a]?			
yes	134/196 (68.4)	62/196 (31.6)	6.9% (−1.0–14.8)
no	279/454 (61.5)	175/454 (38.5)	
qSOFA criteria met[a]?			
yes	13/30 (43.3)	17/30 (56.7)	**20.5% (2.4–38.7)**
no	396/620 (63.9)	224/620 (36.1)	
Reason for antibiotic administration			
treatment	541/812 (66.6)	271/812 (33.4)	5.1% (−3.1–13.3)
prophylaxis	99/161 (61.5)	62/161 (38.5)	
Time that antibiotic was prescribed			
day shift	374/559 (66.9)	185/559 (33.1)	0.6% (−7.3–8.5)
night shift	120/181 (66.3)	61/181 (33.7)	

Values in bold indicate statistical significance.
[a]SIRS and qSOFA criteria were only applied to patients over the age of 18 years who were prescribed antibiotics to treat presumed infection.

approach to the adjudication of antibiotic prescribing in the ED. This contrasts with many previous studies assessing antibiotic appropriateness, where appropriateness has been defined based on culture and susceptibility results.[15–18] Culture results are often both (i) unavailable to the ED clinician at the time of antibiotic prescribing and (ii) often confounded by both false positives (e.g. contamination and colonization) and false negatives.[19–21] Culture and susceptibility test results are often particularly unhelpful (i.e. not required) in patients who are not systemically unwell with their infection[19,20,22–24] and thus a retrospective, culture-based method of assessing antibiotic appropriateness is unsuitable for many patient presentations included in our study.

Antibiotics were found to be a common intervention in the ED, with more than 1 in 8 patient presentations involving the prescribing of one or more antibiotic(s). This study demonstrated that the majority of antibiotics were prescribed to patients who did not meet established criteria (SIRS/qSOFA) for sepsis. There is a prominent research emphasis dedicated to identifying sepsis in the ED with a focus on targeting early initiation of antibiotics.[25] In septic shock, delays in antibiotic administration in the ED have been associated with increased mortality,[26–28] increasing the pressure on clinicians to make early decisions when prescribing antibiotics. However, we hypothesize that the larger cohort of less-sick ED patients (i.e. not meeting any sepsis criteria) who are prescribed antibiotics represents fertile ground for identifying areas more easily amenable to AMS or identifying conditions wherein antibiotics may not be required at all. For example, strong evidence already exists that antibiotics are not required for uncomplicated otitis media,[29] uncomplicated diverticulitis,[30] acute bronchitis,[31] domestic animal bite prophylaxis[32] and simple hand lacerations.[33]

The administration of inappropriate antibiotics in the ED was common, with ∼1 in 3 patients being prescribed an antibiotic regimen that was assessed as either suboptimal or inadequate. The most common reasons that assessors deemed an antibiotic prescription to be inappropriate were that antibiotics were either too broad, there was an unnecessary overlap of spectrum or antibiotics were not required at all. Such overprescribing increases the risk of unnecessary antibiotic-associated adverse events, opportunistic infections [e.g. *Clostridioides* (*Clostridium*) *difficile* infection] and AMR.[2,3] We therefore propose the need for AMS regimens tailored to the ED environment to reduce unnecessary antibiotic exposure. This is particularly important given that the majority of antibiotic regimens prescribed in the ED continue unchanged by inpatient teams after 48 h.[34] It thus follows that antibiotic prescribing in the ED impacts the patterns of antibiotic use across the hospital. Possible AMS strategies include: increasing the presence of ED-based clinical pharmacists; adopting electronic prescribing systems that incorporate clinical decision support tools; and ED-specific antibiogram development.[4,35]

Table 3. Site and assessment of appropriateness for both treatment and prophylactic antibiotic regimens

Site	Appropriate, *n* (%)	Inappropriate, *n* (%)	Not assessed, *n* (%)
Treatment			
abdominal	40/60 (66.7)	16/60 (26.7)	4/60 (6.7)
CNS	4/6 (66.7)	2/6 (33.3)	0/6 (0)
dental	9/26 (34.6)	16/26 (61.5)	1/26 (3.8)
ear/nose/throat	44/105 (41.9)	58/105 (55.2)	3/105 (2.9)
gynaecological	23/32 (71.9)	7/32 (21.9)	2/32 (6.2)
orthopaedic	5/9 (55.6)	2/9 (22.2)	2/9 (22.2)
respiratory	106/160 (66.3)	52/160 (32.5)	2/160 (1.3)
unknown source	22/36 (61.1)	11/36 (30.6)	3/36 (8.3)
skin	150/209 (71.8)	54/209 (25.8)	5/209 (2.4)
urinary	119/159 (74.8)	35/159 (22.0)	5/159 (3.1)
other	19/41 (46.3)	18/41 (43.9)	4/41 (9.8)
Prophylaxis			
bite prophylaxis	18/23 (78.3)	5/23 (21.7)	0/23 (0)
surgical prophylaxis	5/9 (55.6)	3/9 (33.3)	1/9 (11.1)
wound prophylaxis	65/118 (55.1)	45/118 (38.1)	8/118 (6.8)
other prophylaxis	11/21 (52.4)	9/21 (42.9)	1/21 (4.8)
Unknown indication	0/5 (0)	0/5 (0)	5/5 (100)

We also investigated antibiotic appropriateness for pre-defined subgroups of patients. Patients who met qSOFA criteria for sepsis were more likely to be prescribed inappropriate antibiotics than those who did not meet qSOFA criteria. We hypothesize that, for these sicker patients, clinicians are under greater time pressures to administer antibiotics and, consequently, the haste to administer antibiotics may drive inappropriate prescribing. Further research, however, is required to see whether this finding can be replicated and, if so, determine whether an association between time-to-antibiotics and appropriateness of antibiotics exists. The lack of an association between meeting SIRS criteria and antibiotic appropriateness, on the other hand, is unsurprising given that SIRS is a poorer marker of critical illness compared with qSOFA.[36]

Finally, we found that adult patients were significantly more likely to have been prescribed inappropriate antibiotics than children. The reasons for this are unclear and require further exploration. Possible hypotheses may include that antibiotic prescribing decisions in children are simpler owing to fewer comorbidities or, alternatively, there may be an increased reluctance to prescribe medications to this population.

Limitations

This study suffers from the inherent limitations of retrospective design and thus is suited more towards hypothesis generation, rather than determining causal factors that influence the appropriateness of antibiotic prescribing. The single-centre nature of the study may also limit its generalizability. Nonetheless, by using a large number of consecutive patients with few missing data for key variables, this study provides a solid platform for future, multi-centre prospective studies that can replicate our methods. Although we included fewer patients than intended (1019 versus 1333), this did not affect the magnitude of the sample error (2.0% versus 1.8%).

Further, the assessment of antibiotic appropriateness based on data available at the time of ED presentation has the potential to be influenced by inter-assessor variability. We have attempted to minimize this via both (i) defining appropriateness based on a previously established tool designed for this purpose that relies on evidence-based guidelines, and (ii) using a panel of specialists from relevant but diverse backgrounds. We believe that the thoroughness and practical approach to our assessment of appropriateness is a unique strength of this study, which we have detailed in the methodology so that it may be replicated by other investigators. Finally, the present study was purely descriptive in nature and as such we did not aim to quantify what constitutes a clinically relevant difference in proportions of appropriate antibiotic prescribing, since this is likely to be setting-, condition- and patient-specific. However, we hypothesize that even small improvements in appropriate prescribing are likely to lead to relevant patient and health economic outcomes.

In conclusion, our study provides contemporaneous insights into the practice of antibiotic prescribing in the uniquely challenging environment of the ED. Antibiotics were found to be a common intervention in the ED and, with over one in three antibiotic prescriptions being assessed as inappropriate, there is a pressing need to develop initiatives to improve ED-based antibiotic prescribing. We propose the need for future studies that aim to further explore and address factors associated with inappropriate prescribing of antibiotics, in order to reduce unnecessary patient and community antibiotic-related harms.

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Transparency declarations

None to declare.

Supplementary data

Tables S1 and S2 appear as Supplementary data at *JAC* Online.

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