ORIGINAL RESEARCH

Antibiotic guideline adherence by Clinicians in medical wards at Queen Elizabeth Central Hospital (QECH), Blantyre Malawi

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Abstract

Background

Antimicrobial resistance (AMR) is a major concern in health care worldwide. In Malawi rates of AMR, in particular third-generation cephalosporin-resistant (3GC-R) Enterobacterales have rapidly increased since 2003. Antibiotic guidelines are a key component of antimicrobial stewardship (AMS). As part of stewardship, Queen Elizabeth Central Hospital (QECH) in Blantyre, Malawi developed an antibiotic guideline in the form of a smart phone application in June 2016.

Aim

We conducted a study to assess clinicians adherence to the local antibiotic guideline on the adult medical wards, two years after it was introduced. Specifically assessing choice of antibiotic, time of blood culture collection and 48-hour review.

Methods

A cross-sectional study was carried out using purposive sampling method. 230 case files of adult patients were audited against the antibiotic guideline. Adherence to the guideline in terms of indication for antibiotic, choice of antibiotic and antibiotic review time was reviewed. Statistical analysis was done using IBM SPSS and presented with descriptive statistics.

Results

194 (84% [95% CI 79.0-88.8]) antibiotic prescriptions were adherent to the guideline, 28 (12% [95% CI 8.2-17.1]) non-adherent and 8 (3.5% [95% CI 1.5-6.7]) antibiotic indication was not clear. The most common indication for antibiotic prescriptions was pneumonia, as documented in 89 (39% [95 % CI 32.4-45.3]) case files. 191(76% [95% CI 70.3-81.2]) of prescriptions were for ceftriaxone. There was evidence of utilising blood culture to adjust therapy as 88/230 (38% [95% CI 32.0-44.9]) had culture taken. 175(76% [95 % CI 70.0-81.4]) of files had antibiotics reviewed within 48 hours.

Conclusion

There is still need to work on rational prescribing of antibiotics as ceftriaxone usage was high during this study period. Scheduled audits and point prevalence surveys should be implemented quickly to reduce the impact of antibiotic resistance and improve individual patient care.

Keywords: Antibiotic resistance, Antimicrobial stewardship, Antibiotic guideline, sub-Saharan Africa

Introduction

Antimicrobial resistance(AMR) is a major concern in health care worldwide[1]. AMR bacterial infections threaten health care with greatest mortality burden expected to occur in low and middle-income countries (LMICs)[2]. Sub-Saharan Africa (sSA) has the highest rate of AMR in key pathogens[3]. Due to limited nursing capacity, many hospitals in sSA use broad-spectrum antimicrobials with once daily-dosing regimen leading to the widespread adoption of third-generation cephalosporins (3GC) like ceftriaxone for empirical management of blood stream infections(BSI)[4]. In this setting, 3GC-resistant (3GC-R) Enterobacterales pose a threat to the treatment of BSI and Malawi has detected this emerging widespread resistance potentially attributed to overuse[2,5,6].

Antimicrobial stewardship(AMS) is one of the strategies recommended to curb AMR through optimal prescribing of antibiotics by appropriate selection, dosing, route and duration[7,8]. A crucial component of AMS programs is adherence to antibiotic prescription guidelines which guides optimal antibiotic selection[9]. Few studies in sSA have evaluated the appropriate therapeutic antibiotic use[10].

In 2016, Queen Elizabeth Central Hospital (QECH), Blantyre, Malawi introduced an AMS program in adult medical wards that included guideline introduction assessed by two audits and a series of prevalence studies. The guideline was devised by a multidisciplinary team and distributed in form of booklets, posters and a smartphone application[11,12]. It has AMS components for body systems infections and surgical prophylaxis focusing on principles of good antibiotic prescribing and routes of administration precisely switching from intravenous route to oral route, notes on dosing and dose adjustment, alternatives to shortage and stock outs. This study audited the adherence of prescribers to this local antibiotic guideline after two years of its introduction with specific objectives of evaluating if choice of antibiotic given was in line with the guideline, timing of blood culture collection before start of antibiotics and 48 hour review of antibiotics.

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Methodology

Study setting

QECH is a tertiary healthcare facility with 1,500 beds, located in the southern part of Malawi[13]. This study was conducted on the adult medical wards at QECH, which have a total of 200 beds[13]. It provides free inpatient health care to Blantyre district, which has a population of 995,000 (2018 census) and surrounding districts in the southern region. The facility was chosen because the department of medicine had recently produced local antibiotic guideline[11,12].

Study design, Sampling procedure and participants

A cross-sectional study was undertaken where case notes were reviewed and quantitative data on antibiotic prescription was collected from patients' hospital records, prescribing cadres case notes and drug prescription sheets. Using purposive sampling method, patients with rich data for the study were selected. The criteria for patient participants inclusion were those that had been admitted, had antibiotics prescribed for them and been in the ward for at least two days.

Table 1: Social demographics of study population

Variable	Frequency (n=230)	Percentage (%)
Sex		
Male	111	48
Female	119	52
Age group (years)		
15-29	56	24
30-44	92	40
45-59	39	17
≥60	43	19
Median age 40 IQR (30-50)		

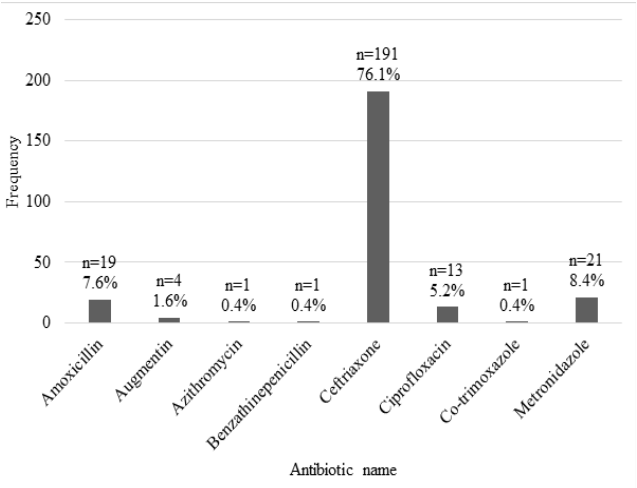

Figure 1: Name of antibiotics prescribed throughout the study period

Table 2: Clinical indication for antibiotics

Indication	Frequency (n=230)	Percentage (%)
CNS	73	31.7
Fungal Meningitis	1	0.4
Neurosyphillis	2	0.9
Presumed Bacterial Meningitis	69	30.0
Toxoplasmosis	1	0.4
Co-infection	1	0.4
Enteric	23	10.0
Acute GE	5	2.2
Ascites and hepatomegaly	1	0.4
Chronic Diarrhoea	4	1.7
NTS	6	2.6
Obstructive Jaundice	1	0.4
PUD	2	0.9
Typhoid	3	1.3
unresolved E.coli	1	0.4
Respiratory	89	38.7
Aspiration Pneumonia	7	3.0
CAP	30	13.0
COPD Exacerbation	5	2.2
Lung Abscess	1	0.4
Pleural effusion	3	1.3
Pneumonia	35	15.2
Severe CAP	1	0.4
Severe Pneumonia	7	3.0
Sepsis	28	12.2
Known Origin	19	8.3
Unknown Origin	9	3.9
Urinary Tract Infection	8	3.5
Simple UTI	5	2.2
Pyelonephritis	3	1.3
No clear Indication	8	3.5
Oral thrush	1	0.4
BPH	1	0.4
Disseminated TB	1	0.4
Neck mass, Lymphoma?	1	0.4
Nosocomial infection	1	0.4
Reactive arthritis	1	0.4
Splenomegaly	1	0.4
Vasculitis	1	0.4

Abbreviations: BPH: Benign Prostatic Hyperplasia, CAP, Community Acquired Pneumonia, COPD: Chronic Obstructive Pulmonary Disease, NTS: Non-Typhoid Salmonella, PUD: Peptic Ulcer Disease, TB: Tuberculosis, UTI: Urinary Tract Infection

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Table 3: Level of cadre in prescribing and reviewing

Grade	Prescriber			Reviewer		
	Frequency (n=230)	Percentage (%)	95% CI	Frequency (n=230)	Percentage (%)	95% CI
Consultant	2	0.9	0.1-3.1	26	11.3	7.5-16.1
Registrar	11	4.8	2.4-8.4	4	1.7	0.5-4.4
Intern	76	33.0	27.0-39.5	45	19.6	14.6-25.3
Clinical Officer	12	5.2	2.7-8.9	1	0.4	0.0-2.4
MBBS year 5 students	6	2.6	1.0-5.6	8	3.5	1.5-6.7
Unknown (missing grade)	123	53.5	46.8-60.1	146	63.5%	56.9-69.7

All records for patients or guardians who did not give informed consent or assent were excluded from the study. A total of 230 case files were reviewed for a period of three weeks during summer season.

Data Collection

Data was collected within a period of three weeks from 6th of September 2018 to 27th of September 2018 using the locally developed AMS audit tool[11]. This was carried out by G.T.S, T.M and S.S and this data was reviewed weekly by a supervising investigator; N.P.K who was not involved in data collection. Data extracted from the case notes and drug sheets included: patients' demographics such as age and sex; medical information on indication for antibiotic, name of antibiotic prescribed, blood culture collection practice before or after initiating antibiotics, documentation of antibiotic duration and review time.

Adherence to local antibiotic guideline: This was assessed by looking at the indication for the antibiotics and the prescribed antibiotic. Analysis focused on whether there was correct dosing, route, time and documentation of the antibiotic given with reference to the local guideline. The clinician was deemed non-adherent if at least one of the listed items were not carried out according to the guideline.

Other factors that were assessed in regards to prescribing of antibiotics were; blood culture collection practice before antibiotic initiation or after or not at all, indication of antibiotic duration, timing for review of antibiotics and the level of cadre of the prescriber and reviewer. The level of cadre was categorised into: consultant-a specialist medical practitioner in certain disease categories who supervises implementation of care and treatment plans by other health care providers; a registrar-a doctor receiving advanced training in a specialist field of medicine to become a consultant; clinical officer-a professional clinician trained in basic competencies in diagnosing and managing medical condition three years post-secondary school education; interns: newly qualified doctors and paramedicals undergoing a period of supervised training to be licenced to practice medicine[14,15,16,17]. The internship program runs for 18 months for medical officer interns and one year for clinical officer interns[17]. Last category was year five medical students who are Bachelor of Medicine, Bachelor of Surgery (MBBS) final year students.

Statistical analysis

Data from the AMS tool was entered into Microsoft Excel 2013 by T.M and S.S and to avoid any errors the entries were then reviewed by N.P.K for validity and this was analysed using Statistical Product and Service Solutions Statistics (IBM SPSS) by G.T.S.

Ethical Considerations

The study was exempted for ethical review by College of Medicine Research and Ethics Committee (COMREC) [UP.07/18/71] because it was deemed a clinical audit by the committee and there was no involvement of human subjects. Permission to conduct the study was granted by the Hospital Director and Head of the Department of Medicine. Consent was obtained from participants to look in their case notes;those who were 18 years and above and were able to communicate and understand signed a written consent form with a signature or thumb print if unable to read or write. Those who were not able to understand and communicate or were less than 18 years of age had to give an assent after their guardian had given consent. The data collected was anonymous and kept on password locked computers only accessible to study investigators.

Results

Study population

A total of 230 medical records were used for the study. Out of the 230, 119 (52%) files were for female patients, 92 (40%) were aged 30-44 and the median age of all patients was 40 (30-50) [Table 1].

Respiratory infections (89/230;39% [95% CI 32.4-45.3]) and central nervous system (CNS) infections (73/230;32% [95% CI 25.8-38.2]) were the most common syndromes recorded by admitting teams while sepsis accounted for about 28/230 (12% [95% CI 8.2-17.1) of recorded diagnoses [Table 2].

Antibiotic prescription

Only 88(38% [95% CI 32.0-44.9]) of the 230 patients had blood culture samples taken. Of these 81/88 (92% [95% CI 84.3-96.7]) had blood samples taken before antibiotic initiation and seven/88 (8.0% [95% CI 3.3-15.7]) after initiation of antibiotics.

A total of 251 antibiotics prescriptions were reviewed during the study period. Ceftriaxone accounted for (191/251; 76% [95% CI 70.3-81.2]), metronidazole for (21/251; 8.4%, [95% CI 5.3-12.5]), amoxicillin for (19/251; 7.6% [95% CI 4.6-11.6]) and ciprofloxacin for (13/251; 5.2% [95% CI 2.8-8.7]) [Figure 1].

Compliance with documentation of prescriber and reviewer grade

Of the 230 case notes reviewed, a high proportion of both prescribers (123; 54% [95% CI 46.8-50.1] and reviewers (146; 64% [95% CI 56.9-69.7]) did not document their grade. Where documented, the greatest proportion of initial antibiotic prescriptions were by interns (76/230; 33% [95% CI 27.0-39.5]) [Table 3]. 175/230 (76% [95% CI 70.0-81.4]) of prescriptions showed evidence of a 48-hour review majority done by interns (45/230; 20% [95% CI 14.6-25.3])

with 65/175 (37% [95% CI 30.0-44.8]) utilising blood culture results during the review.

Adherence to the local guideline

Using all or none criteria, 194/230 (84% [95% CI 79.0-88.8]) of the case notes were deemed to be rational prescription and adhered to the local guideline in terms of clear documentation on indication for given antibiotic, right choice of antibiotics prescribed, right time, right dose, right route. 28/230 (12% [95% CI 8.2-17.1]) were not adherent due to either wrong choice (9/28; 32%) or combination (1/28; 3.6%), wrong time (8/28; 29%), wrong dose (8/28; 29%), wrong route (2/28; 7.1%). 8/230(3.5% [95% CI 1.5-6.7]) had no clear documented indication for antibiotics.

Discussion

With an overall adherence of 84% [95% CI 79.0-88.8] to the local antibiotic guideline for all prescriptions in the audit period, the results show that this quality of care to the standard is already good but can be improved if local stewardship recommendations are considered. Maintaining and improving adherence will potentially be of great importance in not only preventing the emergence of drug resistance, but also enabling effective utilization of resources, bringing down the cost of medical care and most importantly having the best individual treatment outcomes for patients[18].

Unlike high income settings which have shown successful outcomes from introduction of antibiotic guidelines, data from LMICs is limited[19]. AMS programs in South Africa and Kenya showed suboptimal levels of adherence at 45.1% and 53.6% respectively compared to our findings[20,21]. Despite being resource constrained, these settings are very different from Malawi and they carried out their studies in multiple hospitals throughout their countries which were done on a first time basis after the introduction of the guidelines[20,21]. The higher rate of adherence in our context could be attributed to;the survey being done in one facility, in a single department where guidelines were developed, it being a third audit after guideline introduction and clinicians being trained and educated on importance of the AMS program as previous studies have demonstrated benefits of educational intervention[7].

Most studies including ours indicate that unwarranted prescriptions of antibiotics are due to: inaccurate diagnosis, inexact recognition of conditions that can be treated with antibiotics and concerns of poor clinical outcomes if patients are not given antibiotics[22]. In our study, there was a high level of ceftriaxone use. Initially, findings during the implementation of this stewardship program in the same wards showed a significant reduction in ceftriaxone usage over a period of two years but our study showed an increase in ceftriaxone usage from 53.6% [95% CI 48.1-59.1] observed during end of this stewardship program to 76% [95% CI 70.3-81.2][11].

This potential increase in ceftriaxone usage could be attributed to; data being collected over a short period of time with wide confidence intervals in ceftriaxone use, recruitment of new prescriber;ssss interns who might not have been properly oriented to or be familiar with the local antibiotic guideline might have occurred during the same period since QECH is an internship training centre where interns rotate for only three months in Medicine Department. Another attribute to the high usage would be its convenient frequency of administration which is advantageous in understaffed scenarios compared to other antibiotics that require multiple daily doses. Furthermore, our study did not assess the availability of different antibiotics in stock which could also potentially affect usage of one particular antibiotic. In spite of this, a final conclusion cannot be made without point prevalence surveys and repeat audits on a regular basis.

Most of the initial antibiotics are prescribed on admission by on call team which mostly consists of interns and Medicine Department registrars. This has been reflected in our study as interns were majority of prescribing clinicians. It has been shown that hierarchy of a clinician may also affect antibiotic prescription as level of training and clinical experience is crucial in decision making as selection of diagnoses and adherence to guidelines may vary between physicians[23]. Although junior clinicians mostly carry out the actual prescribing process, their seniors often make the decision whether and what to prescribe and this often leads junior clinicians to adopt prescribing behaviours that are inconsistent with the guidelines[24]. Hence forth in addition to providing guidelines, improvement in the supervision of junior clinicians is crucial[25].

Concerning the review of antibiotics which is recommended to be done within 48 hours by either consultant, registrar or intern depending on which day of the week the review happens, it has remained high since the previous survey with interns and registrars taking a leading role. This is of great importance as 48 hour review has shown to reduce duration of therapy without affecting patients' outcome and safety since prolonged or inappropriate antibiotic therapy increases the risk of health-care associated infections, development of resistance and also lengthens hospital stay[11]. Therefore, focus should be put on senior review in terms of broadening their knowledge and awareness towards its importance[26].

Studies have shown that blood culture surveillance influences prescription patterns in terms of guiding selection of appropriate antimicrobial therapy, de-escalation of antibiotic therapy and switching from intravenous to oral therapy[19]. This has a positive effect in improving clinical outcomes, adverse events, reducing costs and length of hospital stay[27]. However, these benefits cannot be achieved if blood cultures are not taken. Challenges such as high cost of investigation services, long turnaround time for follow up and not diligently acting upon results are what affects steady use of blood culture surveillance and this may encourage empirical management of conditions as well as polypharmacy which may further drive resistance[28,29]. Our study showed good timing of blood culture sampling which could be due to QECH benefiting from a sustained access to a quality blood culture service since it is a regional referral laboratory supported by government which could mean lower costs for patients. There was also evidence on adequate use of the results to adjust therapy. Of note, blood cultures are not indicated for all conditions and also some health facilities have blood culture services hence the percentage coverage is acceptable.

Duration of antibiotics was not indicated in majority of the prescriptions during admission. This could be due to the fact that most conditions are empirically managed and antibiotics can be scaled down or stopped anytime depending on patients' state and investigation results on subsequent ward rounds and this aspect might make it difficult to assess adherence. However, failure to indicate antibiotic duration on review ward rounds after a working diagnosis has become apparent poses more threat as a driver of resistance and can also

impact hospital costs as antibiotics will be given for a longer or a shorter period unnecessarily. A study done in a tertiary care government hospital in New Delhi, India confirms that appropriate indication of duration for an antibiotic achieves optimal efficacy in managing infections and has been an important tool in effort to reduce inappropriate use of antibiotics and subsequent development of both resistant micro-organisms and drug related adverse events[18].

Study Limitations

We report one survey done over a short period of time as it was an undergraduate research project with an allocated time frame of four weeks and it took place during a period where new interns were being recruited who might have potentially influenced high ceftriaxone use. In addition, this survey did not capture seasonal variations in disease pattern since some diseases peak in certain seasons; the study happened in summer which is dry and hot. According to Malawi's assessment on climate impacts on health, during hot season there is a peak incidence of droplet infections like CNS infections and allergic reactions from dust particles e.g. upper respiratory tract infections which can be misdiagnosed as pneumonia. This was highlighted in the study as respiratory and CNS infections were the common syndromes for admission of which could portray a different pattern if the survey was carried out in another season. All this had an impact on the choice of antibiotic to be used henceforth limiting the study. Stock outs of essential drugs is inevitable and it affects the availability of the type of drugs to be chosen from. Even though this was not assessed we believe that it might have potentially affected the survey as it was noted that certain conditions were getting the next best antibiotic instead of the first line. Furthermore, the guidelines recommend ceftriaxone usage for severe pneumonia and amoxicillin for non-severe cases, assessment of severity by the investigators was difficult from the clinical records which posed a challenge to the study team when assessing whether the type of antibiotic given was in-line with the guideline. It was also difficult to assess whether choice of antibiotic was according to the local guideline if multiple differential diagnoses of infections were indicated by the admitting clinician. We also acknowledge that clinical specialties which are needed to assess appropriateness of antibiotics did not include clinical microbiologist and pharmacists as engaging them would have been ideal during the study period. Therefore, this shows how adherence is hard to judge retrospectively using medical notes.

Despite these limitations, we believe our findings provide interesting data on adherence gaps which may give guidance to the authorities on potential strategies which can easily be adopted. Strategies such as identifying prescribers with signatory stamps for different clinician cadres to stamp after documenting their notes and prescriptions so they can be traceable would be one of the important aspects to validate. This can make clinicians accountable for their decisions through clear documentation in order to reinforce adherence to the guideline when administering antibiotics as they would be aloof of any consequence that could befall them if they do not appropriately follow guidelines.

Conclusion

Our study showed high levels of adherence to the local antibiotic guidelines. However, good clinical practice in terms of documentation of clinicians level of cadre with legible handwriting needs to be improved to make it easier for future audits. Recommendation in the ward would be to continue to develop the AMS program in the long run. In view of this, scheduled audits and point prevalence surveys should be implemented to reduce the impact of antibiotic resistance and to improve individual patient care through optimal use of antimicrobials. Furthermore, proper orientation and training of new junior clinicians would be required every three months to keep new interns or medical students updated with the guideline.

Abbreviations

AMR: Antimicrobial resistance; LMICs: Low-and middle income Countries; sSA: sub Saharan Africa; 3GC: third generation Cephalosporins; 3GC-R: third generation cephalosporin resistance; AMS: Antimicrobial stewardship; QECH: Queen Elizabeth Central Hospital; MBBS: Bachelor of Medicine Bachelor of Surgery; IBM SPSS: Statistical Product and Service Solutions Statistics; COMREC: College of Medicine Ethics Committee; CI: Confidence interval; CNS: Central nervous system.

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Conflict of Interest

All authors declare that they have no competing interest related to this work conflict. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Authors' Contribution

N.P.K and R.L were responsible for devising, designing and supervising the study. G.T.S, T.M, S.S collected data and had full access to the data. G.T.S conducted statistical analyses. All authors were involved in interpretation of the analyses and write up of both initial and final versions of the manuscript. All authors revised and reviewed the manuscript critically for important intellectual content.

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