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Antimicrobial Use Among Outpatients at Benjamin Mkapa Hospital in Dodoma Central Zone of Tanzania: A Prospective Descriptive Study

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ABSTRACT

Objective: Irrational antimicrobial use (AMU) has led to an exponential increase in antimicrobial resistance (AMR) in hospitals and communities, which creates challenges in treating infectious diseases caused by bacteria. This study aimed to evaluate antimicrobial prescriptions and usage patterns for treating bacterial infections among outpatients at Benjamin Mkapa Hospital (BMH).

Materials and Methods: A prospective descriptive study design was used to evaluate the AMU trend. The data were collected from August 2022 to October 2022 from outpatient pharmacies at BMH using the World Health Organization/International Network of Rational Use of Drugs (WHO/INRUD) indicators. The simple random sampling method was employed to select the prescriptions. The WHO AWaRe (Access, Watch, and Reserve) classification was used to classify common antimicrobials. We analyzed the prevalence of outpatient AMU, including the types of antimicrobials, indications, and compliance with treatment guidelines. We also examined the number of antimicrobials per prescription and the adherence to drug use.

Results: We examined 1557 prescriptions, 406 (26.1%) (WHO recommendation 20.0-26.8%) of which included antimicrobials. All prescriptions with antimicrobials were written in generic names, drug utilization-90% (DU90%) was 100% (WHO recommendation 100%). The number of parenteral antimicrobials prescribed was 79 (19.5%) (WHO recommendation 13.4-24.1%). Furthermore, prescriptions with antimicrobials that complied with the current Standard Treatment Guidelines and National Essential Medicine List in Tanzania (STG/NEMLIT) were 369 (90.9%) (WHO recommendation 100%). Most antimicrobials were presc-

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ribed as monotherapy, accounting for 265 (65.3%). There were 1.4 (WHO recommendation 1.6-1.8) antimicrobials per prescription. Our study identified 21 commonly prescribed antimicrobials, whereby 9 (42.9%) (WHO recommendation >60%) antimicrobials were Access, 10 (47.6%) (WHO recommendation <20%) Watch, and 2 (9.5%) (WHO recommendation <1%) Reserved classes.

Conclusion: Our study showed that BMH has optimal practices for prescribing and using antimicrobials for outpatients. It further underlined the need to expand and strengthen antimicrobial stewardship efforts to reinforce prescribing antimicrobials.

Keywords: antimicrobial use, antimicrobials, WHO/INRUD indicators, AWaRE classification, antimicrobial stewardship, antimicrobial resistance

INTRODUCTION

Antimicrobial resistance (AMR) is declared one of humanity's top ten global public health threats (1). AMR is associated with increased hospitalizations, extended hospital stays, readmissions, and a higher mortality risk (2). In 2019, 4.95 million deaths, including 1.27 million directly attributable, were associated with bacterial AMR. Sub-Saharan Africa has the highest all-age death rate attributable to AMR at 27.3 deaths per 100,000 (3). In 2015 and 2017, the WHO and Tanzania Mainland Ministry of Health launched the Global and National Action Plans for AMR with five goals: raising awareness and sharing accurate information, improving surveillance and research, reducing infections, enhancing the proper use of antimicrobial agents, and creating a strong economic rationale for sustainable investments. In 2023, Tanzania added a sixth goal to improve coordination and governance in combating antimicrobial resistance (4-6).

Irrational drug use, particularly antimicrobials, is the primary drive accelerating the increase of AMR (7, 8). In low- and middle-income countries, there has been a reported significant rise in antimicrobial use (AMU) and consumption in recent decades (9). Regular AMU surveillance improves knowledge and prescription practice among healthcare providers, fostering advanced, rational prescribing and use of antimicrobials (10). Thus, AMU is identified as a particularly indispensable target for surveillance interventions (11). Several tools have been developed to serve this purpose. It is essential to survey prescribing tendencies and the use of antimicrobials in outpatient and emergency care departments because they serve many patients, and most prescriptions happen there (12).

The World Health Organization/International Network of Rational Use of Drugs (WHO/INRUD) indicators are surveillance tools used to understand the pattern of AMU in outpatients (13). It measures prescribing performances for health facilities. Several studies assessed AMU using the WHO/INRUD indicators. A study in Kenya, an East African country, conducted AMU surveillance using the WHO/INRUD indicators from rural counties in ten public primary healthcare centers. Of all prescriptions assessed, 84.8% had antimicrobials prescribed higher than the recommendation by WHO (20.0-26.8%). Prescription of injection was 24.9% (recommended 13.4-24.1%), and the almost optimal percentage of prescribed drugs from the Kenya Essential Medi-

HIGHLIGHTS

- This is the first study to use the World Health Organization/International Network of Rational Use of Drugs (WHO/INRUD) indicators to monitor antimicrobial use in outpatients at a central zonal referral hospital in Tanzania.
- This study was conducted after implementing the first National Action Plan on Antimicrobial Resistance (NAP-AMR).
- This study's sample size was large enough to reflect the prescribing and using antimicrobials at Benjamin Mkapa Hospital.

cines List was 96.7% (recommended 100%) (14). In Tanzania, several studies have assessed AMU, antimicrobial consumption (AMC), and AMR, leading to interventions and establishing antimicrobial stewardship teams; however, limited data is available on prescribing antibiotics in Tanzanian hospitals, especially in tertiary hospitals for outpatients. Even though outpatients represent about 90% of all AMU, with more than half of these prescriptions being either unnecessary or inappropriate (12, 15) no adequate studies have been conducted on AMU using the WHO/INRUD indicators or outpatient and emergency care for tertiary zonal referral hospitals. Our study, conducted at a tertiary and zonal referral hospital in the central zone of Tanzania, aimed to analyse antibiotic prescribing practices and trends among outpatients to provide valuable insights for developing successful antimicrobial stewardship initiatives using the WHO/INRUD indicators.

MATERIALS AND METHODS

This prospective descriptive study was conducted at Benjamin Mkapa Hospital (BMH), a tertiary and zonal referral hospital in the central zone of Tanzania, with nearly 400 beds capacity. AMU data for outpatients were collected from August 01 to October 31, 2022, using the WHO/INRUD indicators to investigate drug use in health facilities (13). Data were collected prospectively daily for three consecutive months (August, September and October).

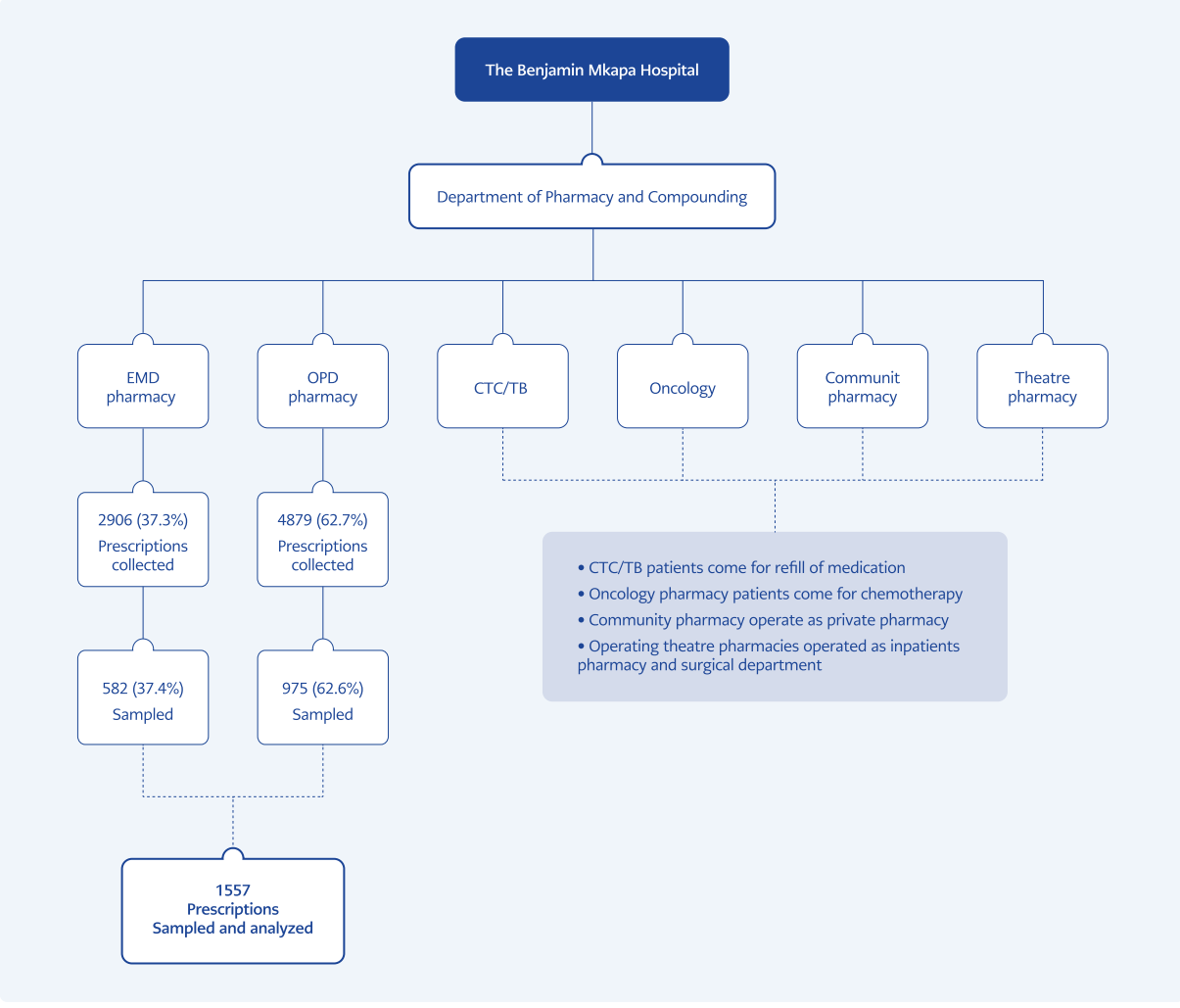

Figure 1. A flow chart showing a sampling of prescriptions from EMD and OPD pharmacies.

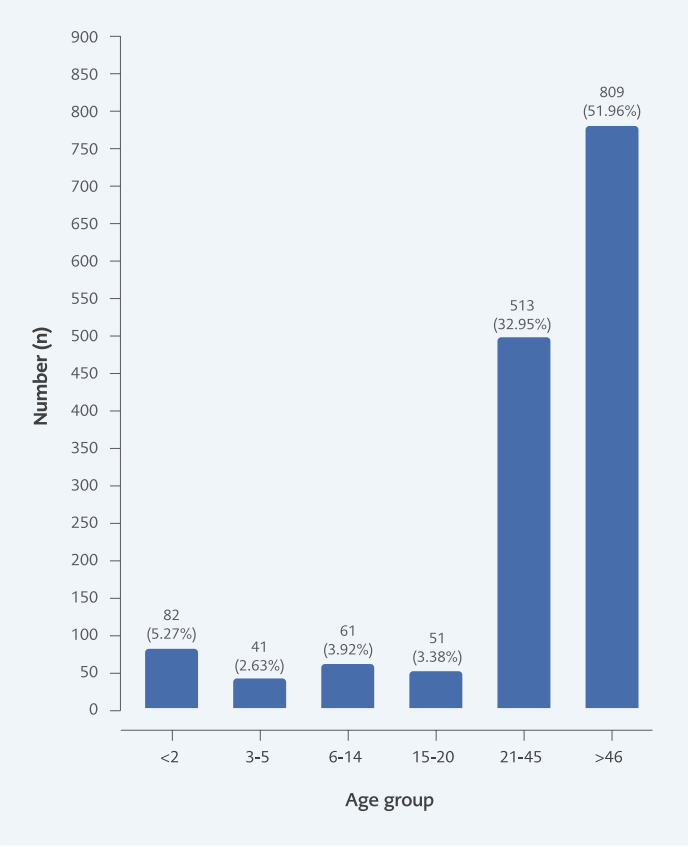

Figure 2. Age group description of prescriptions surveyed (N=1557).

The simple random sampling method was used to select the samples, and every fifth prescription was selected in chronological order to obtain at least 600 prescriptions from the outpatients' clinics and emergency department pharmacies as advised by the WHO/INRUD indicators (13). The variables of this study were determined according to the WHO/INRUD indicators. Demographic variables, such as age and sex, were also collected. The indicators presented in Supplement 1 were used to assess AMU in outpatients.

AMU data from pharmacies in the outpatient department (OPD) and emergency department (EMD) were collected. We excluded all inpatient prescriptions. The statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) 20.0 (IBM Corp., Armonk, NY, USA). Tables and chats were used in data presentation to disseminate and publish data on AMU.

The National Institute for Medical Research and the National Health Research Ethics Review Committee (NatHREC) granted the study an ethical clearance certificate with reference number NIMR/HQ/R. 8a/Vol. IX/4260. The decision date was March 31, 2023, and the BMH authority permitted the research to be conducted in the hospital.

RESULTS

A total of 1557 prescriptions were sampled and analyzed. Of these, 975 (62.6%) were from OPD, and EMD 582 (37.4%) pharmacies (Figure 1). Most patients who attended OPD and EMD pharmacies were above 40 years old (Figure 2).

About 26.1% of surveyed prescriptions included antimicrobials (Table 1). Of these, 90.9% complied with current National Treatment Guidelines. Most antimicrobials are prescribed as a single antimicrobial, with 65.3% out of all assessed prescriptions, while about 19.5% of all prescriptions with an antimicrobial presented with parenteral. The total number of antimicrobial items prescribed was 569. The number of prescriptions with antimicrobials was 406, which implies 1.4 antimicrobials per prescription.

These were classified into 21 groups, according to the WHO AWaRE (Access [A], Watch [W], and Reserve [R]) classification and route of administration (Parenteral (P) and Oral [O]). We identified 9 (42.9%) antimicrobials as an A, 10 (47.6%) W, and 2 (9.5%) were R. The top five used antimicrobial were ceftriaxone (P, W) 139 (24.4%), metronidazole (P, A) 109 (19.2%), metronidazole (O, A) 47 (8.3%), ciprofloxacin (O, W) 39 (6.9%) and ampicillin/cloxacillin (O, A) 38 (6.7%). While reserved antimicrobials were used with less than 1% (Table 2). Ampicillin-cloxacillin fixed-dose combination (FDC) (O) and flucloxacillin-amoxicillin FDC (O) were highly prescribed antimicrobial combinations.

Results from this study indicated nitroimidazole derivatives were highly prescribed at 156 (38.4%), followed by penicillin and third-generation cephalosporin at 147 (36.2%) and 144 (35.5%), respectively. In contrast, aminoglycoside, sulfonamide, tetracycline, first-generation cephalosporin, glycopeptide, second-generation cephalosporin, and carbapen-

Table 1. Demographics and prescribing patterns of antimicrobials for outpatients (N=1557).

Variables	n (%)
Gender	
Male	718 (46.1)
Female	839 (53.9)
Proportion of antimicrobials prescription and use	
Antimicrobials	406 (26.1)
No antibiotics	1151 (73.9)
Proportion of prescriptions with antimicrobials (n=406)	
Single antimicrobials	265 (65.3)
Two antimicrobials	128 (31.5)
Three antimicrobials	10 (2.5)
Four antimicrobials	3 (0.7)
Route of administration in prescriptions with antimicrobials (n=406)	
Oral antimicrobials	327 (80.5)
Parenteral antimicrobials	79 (19.5)
Record of indication for antimicrobials prescribed (n=406)	
An indication recorded	391 (96.3)
No indication recorded	15 (3.7)
Prescriptions with surgical prophylaxis indication (n=406)	
Post-surgical follow-up with duration single dose	86 (21.2)
Post-surgical follow-up prescriptions (%) with duration=1 day	15 (3.7)
Post-surgical follow-up prescriptions (%) with duration >1 day	11 (2.7)
Antibiotic prescription compliance with guideline SGT/NEMLIT (n=406)	
Complied with SGT/NEMLIT	369 (90.9)
Not complied with SGT/NEMLIT	37 (9.1)
Drug utilization 90% (DU90%) Number of antimicrobials prescribed in generics (n=569) divided by a total number of antimicrobial items prescribed (n=569) times 100	N/A (100)
The average number of antimicrobials prescribed per patient encountered The number of antimicrobials prescribed in generics (n=569) divided by a total number of prescriptions with antimicrobials (n=406)	1.4 (N/A)

STG/NEMLIT: Standard Treatment Guidelines and National Essential Medicine List.

Table 2. Antimicrobial use and AWaRe classification among outpatients at BMH hospital*.

Rank	ATC CODE	Antimicrobial prescribed (N=569)	AWaRE	n (%)
1	J01DD04	Ceftriaxone (P) 1000 mg	Watch	139 (24.4)
2	J01XD01	Metronidazole (P) 500 mg**	Access	109 (19.2)
3	J01XD01	Metronidazole (O) 200 mg**	Access	47 (8.3)
4	J01MA02	Ciprofloxacin (O) 500 mg**	Watch	39 (6.9)
5	J01CA51	Ampicillin/Cloxacillin (O) 500 mg, 250 mg / 5 mLs**	Access	38 (6.7)
6	J01CR02	Amoxicillin/Beta-Lactamase Inhibitor (O) 625 mg, 375 mg, 156.25 mg / 5 mLs, 228 mg / 5 mLs**	Access	37 (6.5)
7	No Code	Flucloxacillin/Amoxicillin (O) 500 mg	Access	37 (6.5)
8	J01FA10	Azithromycin (O) 250 mg, 500 mg	Watch	31 (5.4)
9	J01MA02	Ciprofloxacin (P) 500 mg	Watch	18 (3.2)
10	J01CR05	Piperacillin/Beta-Lactamase Inhibitor (P) 4500 mg**	Watch	13 (2.3)
11	J01CR02	Amoxicillin/Beta-Lactamase Inhibitor (P) 1200 mg	Access	10 (1.8)
12	J01CA51	Ampicillin/Cloxacillin (P) 500 mg**	Access	9 (1.6)
13	J01GB03	Gentamycin (P) 40 mg / 1mL	Watch	7 (1.2)
14	J01AA02	Doxycycline (O) 100 mg	Access	5 (0.9)
15	J01FA09	Clarithromycin (O) 500 mg	Watch	5 (0.9)
16	J01EE01	Sulfamethoxazole/Trimethoprim (O) 480 mg	Watch	5 (0.9)
17	J01DB01	Cefalexin (O) 250 mg, 500 mg	Access	4 (0.7)
18	J01DD08	Cefixime (O) 200 mg, 400 mg	Watch	4 (0.7)
19	J01DH02	Meropenem (P) 1000 mg	Reserve	3 (0.5)
20	J01FA01	Erythromycin (O) 250 mg	Access	2 (0.4)
21	J01CE02	Phenoxymethylpenicillin (O) 250 mg	Access	2 (0.4)
22	J01CE01	Benzylpenicillin (P) 5,000,000 U	Access	1 (0.2)
23	J01DD01	Cefotaxime (O) 1000 mg	Watch	1 (0.2)
24	J01DC02	Cefuroxime (O) 250 mg	Watch	1 (0.2)
25	J01XA01	Vancomycin (P) 500 mg	Reserve	2 (0.2)
The AWaRe classification of antibiotics (21 antibiotics molecules, denominator)				
1	Access (A)			9 (42.9)
2	Watch (W)			10 (47.6)
3	Reserve (R)			2 (9.5)

N: The number of total antibiotic items from all prescriptions surveyed, **O:** Oral; **P:** Parenteral

*The AWaRE classification is based on the Standard Treatment Guideline of the Tanzania Mainland, 6th ed. 2021.

**Counted once the antimicrobials are due, the same molecules have different dosage forms.

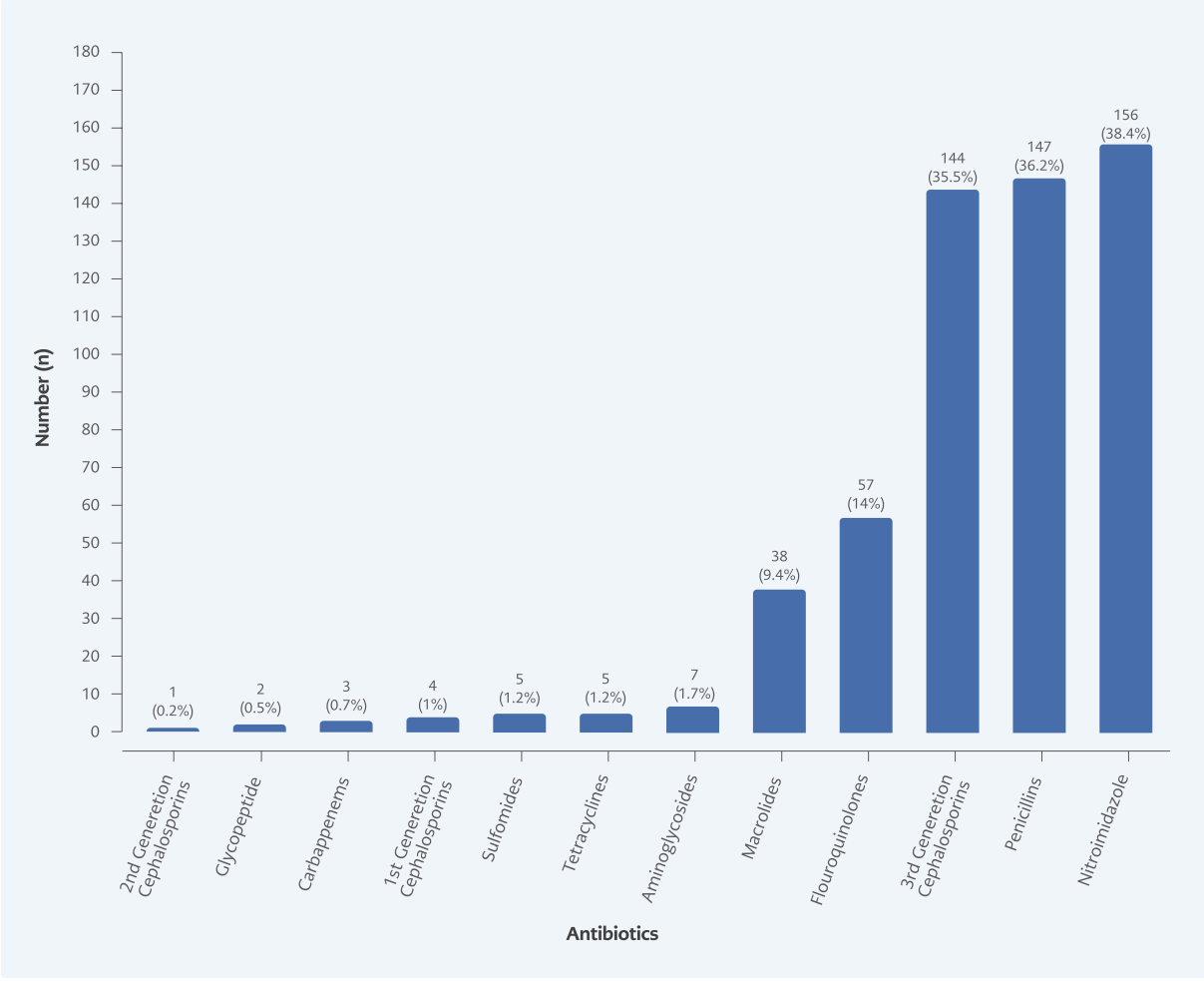

Figure 3. Illustration of classes of antimicrobial prescribed for outpatients.

ems are the least prescribed antimicrobials, which occupied less than 1% of use (Figure 3).

The most typical indications were post-surgical follow-up and urinary tract infection, with 112 (27.6%) and 52 (12.8%), respectively; cough was next at 38 (9.4%), while septicemia and soft tissue infections had 35 (8.6%) (Table 3). The surveillance assumed that each prescription had only one indication.

DISCUSSION

Our study found that BMH has achieved 100% drug utilization with all prescribed antimicrobials in generic names, complying with WHO recommendations (16). The hospital uses the Integrated Health Management Information System (IHMIS) for prescribing and has a formulary to guide medicine-related processes, including antibiotics. The practice at BMH is better than primary care and regional hospitals in Tanzania, with DU90% of 84.4% and 87.5%, respectively (12,17). We found the prevalence of AMU to be 26.1%, and items per prescription were 1.4 (recommended 1.6-1.8) (18, 19). The BMH is a referral hospital, so it was expected to have more antimicrobial prescriptions (14). Fortunately, fewer antimicrobial prescriptions were observed among outpatients. The WHO/INRUD drug use indicators recommend the percentage of prescriptions with an antimicrobial to be 20.0-26.8% (18, 19). A recent study in Kenya reported that 30.02% of all prescriptions contained antimicrobials, and an average of 2.9 antimicrobials were prescribed per each prescription encountered (20).

Table 3. Indication of antimicrobials prescribing for outpatients (N=406).

Rank	Indications	n (%)
1	Post-surgical follow-up	112 (27.6)
2	Urinary tract infections	52 (12.8)
3	Cough	38 (9.4)
4	Soft tissue infections	36 (8.9)
5	Septicaemia	35 (8.6)
6	Pneumonia	31 (7.6)
7	Other upper respiratory tract infections	24 (5.9)
8	Peptic ulcers and oesophageal varices	15 (3.7)
9	No indication	15 (3.7)
10	Gastroenteritis and colitis	11 (2.7)
11	Congestive heart failure	9 (2.2)
12	Genital tract and pelvic infections	5 (1.2)
13	Anaemia	4 (1.2)
14	Diabetic mellitus	4 (1)
15	Sickle cell disorder	3 (0.7)
16	Congenital hydrocephalus and spina bifida	2 (0.5)
17	Cirrhosis of the liver and ascites	2 (0.5)
18	Viral infection	1 (0.3)
19	Spastic cerebral palsy	1 (0.3)
20	Senile cataract	1 (0.3)
21	Patent ductus arteriosus	1 (0.3)
22	HIV disease and histoplasmosis	1 (0.3)
23	Diverticular disease of large intestine and haemorrhoids	1 (0.3)
24	Congenital posterior urethral valves	1 (0.3)
25	Brucellosis	1 (0.3)

N: The number of surveyed prescriptions with antibiotics.

Furthermore, we found that prescriptions including single antimicrobial were 65.3%, two antimicrobials 31.5%, three antimicrobials 2.5%, and four antimicrobials 0.7%. In Pakistan, a study found that 65.1% of prescriptions contained one antimicrobial, 30.6% contained two, and 4.1% contained three. The study suggested that the high prescribing rates of antimicrobials could be due to better clinical outcomes, excessive stock, or aggressive promotion strategies by pharmaceutical companies (21). The comparison was seen in a Jordanian study, which indicated that out of all prescriptions with antimicrobials, 88% had one, 11% had two, and 1% had three antimicrobials (22). The BMH's antimicrobials prescription rate is nearly two-thirds lower than that of Kenya, Pakistan, and Jordan (20-22).

We observed that antibiotics prescribed at BMH followed the WHO recommendation of no more than two antimicrobials per prescription. This may be attributed to the availability of hospital formulary, clinical auditing, internal and external supervision, and health insurance reimbursement restrictions. These factors greatly influence rational prescribing and contribute to fewer antibiotic prescriptions. This study revealed few prescriptions contained parenteral antimicrobials. The WHO recommends 100% compliance with STG/NEMLIT and 13.4-24.1% of parenteral antimicrobial prescribing (1, 19) In this study, the BMH showed 91% compliance with STG/NEMLIT. The prescribing oral and parenteral antimicrobials was within WHO recommendation. The study in Kiisi county Kenya, displayed 96.7% compliance with national essential medicine list i.e higher than our study. Additionally oral and parenteral antimicrobial prescription was 84.8% and 24.9% respectively (14).

Notably, 96% of prescribed antimicrobials had a clear indication for use, with common indications being post-surgical follow-up, urinary tract infections, and cough. It is concerning that antimicrobials are being used for viral infections and coughs. Fever and cough symptoms are not always due to bacterial infections and often do not require antimicrobial treatment (23). The use of parenteral antibiotics for outpatients is common in tertiary hospitals such as BMH. They are often prescribed for post-surgical follow-up and cancer patients with septic wounds, as well as for those undergoing skin procedures or at risk of acquiring infections. Establishing an Outpatient Parenteral Antimicrobial Therapy Patient Management System (OPAT-PMS) to regulate the use of parenteral antibiotics in outpatients is recommended, as it is not widely implemented in public health facilities in Tanzania. We observed prescriptions of parenteral antimicrobials with a stat and single-dose

were 21%, 4% of 24-hour duration, and 3% more than one day. The most common parenteral antimicrobials were ceftriaxone (24%) and metronidazole (19.2%). Other top prescribed antimicrobials included oral metronidazole (8.2%), ciprofloxacin (6.9%), ampicillin/cloxacillin (6.7%), amoxicillin/clavulanic acid (6.5%), flucloxacillin/amoxicillin (6.5%), and azithromycin (5.4%). In Ethiopia, the most commonly prescribed antimicrobials were penicillin G (28.4%), ceftriaxone (24.9%), and cloxacillin (12.84%) (21).

In Tanzania, ceftriaxone is not the preferred first-line treatment for infectious diseases like urinary tract infections due to local evidence of resistance. It has been reclassified as a Watch category antimicrobial. It should generally only be used as a first-line treatment in cases where nitrofurantoin has failed against confirmed severe infections, and sensitivity testing is essential before prescribing (24). The use of ceftriaxone is influenced by its high potency, broad spectrum of activity, low risk of toxicity, and treatment of various bacterial infections. It offers comprehensive pathogen coverage, easy administration, and cost-effectiveness compared to other parenteral antibiotics (23). A similar study found that ceftriaxone, piperacillin/tazobactam, amikacin, and amoxicillin/clavulanic acid were commonly prescribed for pediatric conditions. For post-surgical follow-up in general surgery, obstetrics-gynecology, and orthopedics, cefotaxime, gentamicin, amikacin, and metronidazole were widely prescribed. Tetracyclines are recommended for community-acquired infections (25).

At BMH, four commonly prescribed antimicrobial combinations are ampicillin/cloxacillin, 6.7%, flucloxacillin/amoxicillin 6.5%, ampicillin/cloxacillin 1.6%, and sulfamethoxazole/trimethoprim 0.9%. The preference for these combinations is based on synergism, empirical therapy for poly-microbial infections, and preventing AMR (21, 26). Usually, synergistic effects of antimicrobial combinations are desired when there are high risks of therapeutic failure with individual antimicrobials or a greater probability of developing resistant strains (27). Recent studies refute this argument by reporting synergistic combinations that may enhance the development of resistant strains (4, 28). Other associated risks with antimicrobial combinations include the development of superinfections, more significant toxicity, and an increased financial burden (21). These combinations have also been discouraged by WHO (29).

Our study had some limitations. First, it was conducted over three consecutive months, giving a partial picture of antibiotic use and AMU throughout the year, including seasonal variations. Second, the results cannot be compared to similar local studies in tertiary zonal referral hospitals. Therefore, further prospective or retrospective studies are needed in specialized hospitals in Tanzania to consider seasonal variations.

In conclusion, our study emphasizes the need to strengthen advanced antimicrobial stewardship approaches and recommends further studies in specialized hospitals in Tanzania. Our study further highlights optimal prescribing practices at BMH and recommends instigating the OPAT-PMS at public health facilities to regulate parenteral AMU in outpatients.

Ethical Approval: The National Institute for Medical Research and the National Health Research Ethics Review Committee (NatHREC) granted the study an ethical clearance certificate with reference number NIMR/HQ/R. 8a/Vol. IX/4260. The decision date was March 31, 2023, and the BMH authority permitted the research to be conducted in the hospital.

Informed Consent: N.A.

Peer-review: Externally peer-reviewed

Author Contributions: Concept – K.B.Z., Y.J.Y., M.M.S., C.A.C., A.B.C., M.M.M.; Design – K.B.Z., Y.J.Y., O.S.K., M.M.M.; Supervision – K.B.Z., A.B.C., H.S.K.; Fundings – K.B.Z., H.S.K., C.A.C.; Data Collection and/or Processing – Y.J.Y., O.S.K., K.B.Z., C.A.C.; Analysis and/or Interpretation – K.B.Z., D.A.M., R.S.M., M.M.S.; Literature Review – K.B.Z., M.M.S., A.B.C., H.S.K.; Writer – M.M.S., D.A.M., R.S.M., K.B.Z., Y.J.Y.; Critical Reviews – KBZ., M.M.S., D.A.M., R.S.M., O.S.K., Y.J.Y., C.A.C., A.B.C., H.S.K., M.M.M.

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