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Original Article

Analysis of patterns of antibiotic prescribing in public health facilities in Nepal

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Abstract

Introduction: Inappropriate use of antibiotics is recognised as a leading cause of antibiotic resistance. Little is known about antibiotic prescribing practices at public health facilities in low- and middle-income countries. We examined patterns of antibiotic prescribing in public health facilities in Nepal and explored factors influencing these practices.

Methodology: A cross-sectional study of antibiotic prescribing in public health facilities was conducted in the Rupandehi district of Nepal. Six public health facilities were selected based on WHO guidelines, and data were extracted from administrative records for 6,860 patient encounters. Patterns of antibiotic prescribing were investigated using descriptive statistics. Chi-squared tests and logistic regressions were applied to explore factors associated with antibiotic prescribing.

Results: Of patients attending public health facilities, the proportion prescribed at least one antibiotic (44.7%) was approximately twice the WHO recommended value (20.0 to 26.8%). The antibiotic prescribing rate for hospital inpatients (64.6%) was higher than for other facilities, with the prescribing rate also high in primary health care centres (50.4%) and health posts (52.2%). The most frequently (29.9%) prescribed antibiotic classes were third-generation cephalosporins. Females ($p = 0.005$) and younger ($p < 0.001$) patients were more likely to be prescribed antibiotics. High prescribing rates of antibiotics for selected diseases appeared contrary to international recommendations.

Conclusion: Antibiotic prescribing in public health facilities was high compared with WHO guidelines, suggesting the need for strategies to reduce misuse of antibiotics. This study provides useful information to assist in formulating policies and guidelines to promote more appropriate use of antibiotics in Nepal.

Key words: antibiotic use; antibiotic prescribing; antibiotic resistance; public health facility; Nepal.

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Introduction

Increasing bacterial resistance to antibiotics is a serious threat to health care systems globally [1,2]. Antibiotic resistance occurs when bacteria change in some way that reduce the effectiveness of drugs or other agents designed to cure or prevent infections [3]. Inappropriate antibiotic use is an important contributor as it clearly drives the evolution of resistance [4]. Studies conducted worldwide have shown that antibiotics are frequently used inappropriately [5-7]. In the United States and Canada, 30 to 50% of antibiotic prescription is inappropriate [8,9]. Similarly, in some Asian and African nations, 50% of antibiotic use has been identified as inappropriate [7].

The definition of inappropriate antibiotic prescribing varies between studies [10], making comparisons difficult. A common indicator is the prescription of an antibiotic that is not recommended in prescribing guidelines. As sufficient information about patients' conditions is often unavailable, the World Health Organization (WHO) proposed a standard measure of "*percentage of encounters with an antibiotic prescribed*" in order to assess inappropriate prescribing [11,12]. This measure has been used widely to assess the quality of antibiotic prescribing in health care delivery. However, this proportion is likely to vary according to the mix of presentations to health care. Monitoring the use of antibiotics in countries, assessing factors that promote the inappropriate use of antibiotics and developing effective interventions are important in slowing the pace of resistance development [2,13].

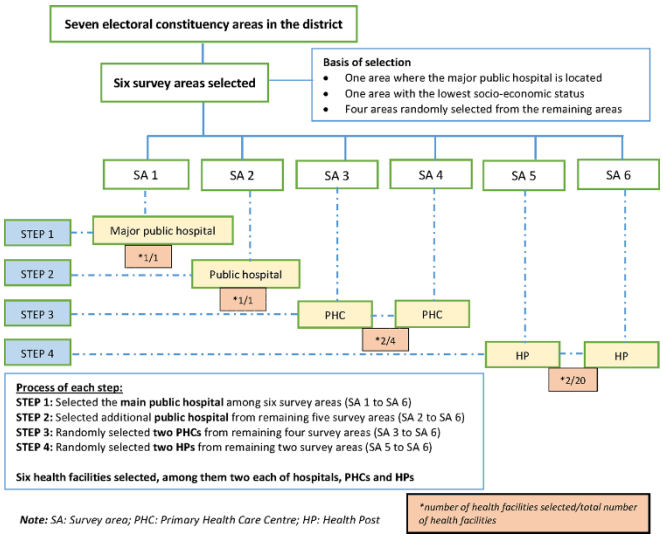
Antibiotics are commonly prescribed and frequently used to treat infections [14]. A substantial amount of antibiotic overuse is likely driven by over diagnosis of certain conditions, particularly when the clinical picture of viral or bacterial aetiology is similar [15]. In developing countries, other factors contributing to the excessive use of antibiotics include inadequate

patient education, limited diagnostic facilities, the availability of antimicrobials that can be purchased without a prescription, and lack of appropriate drug regulatory mechanisms [16]. A strong policy together with strict guidelines, access to diagnostic tests and training about diagnosis and appropriate treatment are factors likely to promote more appropriate use of antibiotics [7].

In Nepal, guidelines for the treatment of childhood illnesses, malaria, tuberculosis, leprosy and human immunodeficiency virus (HIV) infection [17] exist. The antibiotics recommended in the guidelines for those conditions are supplied through the government health system. Similarly, the Government of Nepal has also formulated the National Antibiotic Treatment Guidelines 2014 [18], however not all antibiotics listed in the guidelines are currently supplied through the government system. Thus, public health facilities have limited choices of antibiotics for different diseases. Furthermore, strict regulation and enforcement of appropriate antibiotic prescribing is lacking in the Nepalese health system, thus facilitating failure to follow the guidelines by prescribers. Similarly, several reports have suggested high [19-21] and increasing [22] prevalence of antibiotic resistance in Nepal.

Assessments of drug use within public health care facilities in Nepal have been conducted in individual studies [23,24]. However, these surveys have not assessed appropriate antibiotic use across all levels of health care facilities. In the public health system in Nepal, primary health care services are provided at district level through health posts, primary health care centres and district hospitals, and secondary and tertiary care is provided by zonal/regional hospitals and specialized tertiary facilities [25,26]. Prescribing is conducted by physicians and non-physicians such as health assistants (post-secondary training in diagnostics and therapeutics), nurses and other paramedics [27]. The physicians work at hospitals and the non-physicians, who are referred to as health workers, mainly work at primary health care centres and health posts. Authorities for prescribing drugs and training differ among the prescribers [28], thus their prescribing patterns need to be monitored regularly [29]. In addition to differences between prescribers, drug choice may be influenced by patients, health facilities and other factors [30]. The present study examined the patterns of antibiotic prescribing across different types of public health facilities in Nepal and explored factors influencing these practices.

Figure 1. Flow chart of selection of public health facilities.



Methodology

Selection of health facilities

A cross-sectional study was conducted in the Rupandehi district of Nepal. Public health facilities were selected based on WHO guidelines [31,32]. These guidelines provide a systematic method for assessing the pharmaceutical situation, medicine prices and availability at the country, regional and facility levels. Based on these guidelines, six survey areas were selected from the seven electoral areas in the district. As in the guidelines, the district in which the major hospital is located was selected as one survey area and an area with the lowest socio-economic status as another survey area. An additional four survey areas were randomly selected. One public health facility was selected from each survey area using a list obtained from available records of the District Public Health Office. Six public health facilities were selected, two each of hospitals, primary health care centres and health posts, with the major hospital included as one of the hospitals (Figure 1).

Data collection

Administrative records for a single encounter of outpatients (outpatients of general medicine at hospitals and all from other health facilities), inpatients and emergency department patients irrespective of patient age and diagnosis were collected between July 2017 and December 2017 using a standardised data collection tool. Data extracted from the administrative records, which were paper-based, included patient's sex, age, diagnosis and prescribed medicines. To select the administrative records, data for the most recent year (Nepali year 2073) was divided into four main climate seasons [33]. Data for the middle week of each season

was extracted for each site. If any public holidays were observed in the sampled week, these days were replaced with records of days following the end of the week.

To ensure confidentially, patients' names were not recorded, but the record indexing system used by the health facilities were adapted in generating codes that allowed only the research team to be able to link the extracted records with the source data. Once information for each patient had been checked twice by the principal researcher (AN), the indexing system was de-coded so that the extracted data could not be re-identified.

The principal researcher coordinated data collection and approached respective authorities and health facilities to obtain approval to collect the data, and research assistants were engaged in data collection. A training session for research assistants was held prior to embarking on data collection and focused on the aim of the study, quality in the data collection and ethical considerations. The research assistants were regularly monitored by the principal researcher to ensure the quality of the data through observation at the study sites and cross-checking of the extracted records.

Table 1. Patient characteristics and prescribing indicators.

Variables	Percentage	n_i/n_k[a,b]
Medicine prescribed		
Yes	81.4	5582/6860
No or uncertain	18.6	1278/6860
Sex		
Male	41.3	2833/6859
Female	58.7	4026/6859
Age group		
Less than 5 years	5.2	360/6860
5 to 14 years	14.5	992/6860
15 to 24 years	20.1	1376/6860
25 to 44 years	29.9	2050/6860
45 to 64 years	18.7	1282/6860
65 and above years	11.7	800/6860
Type and department of health facility		
Inpatient hospital	12.6	865/6860
Ambulatory hospital	28.1	1928/6860
Emergency department hospital	29.9	2052/6860
Primary health centre	13.8	950/6860
Health post	15.5	1065/6860
Disease and conditions		
Fever/pyrexia	9.9	681/6860
Cellulitis/boils/impetigo/dermatitis/wound/skin infection/abscess	6.0	413/6860
Falls/injury	5.9	406/6860
Abdominal pain/nausea/vomiting/dyspepsia	5.7	388/6860
ARI/URTI/LRTI/respiratory infection/chest infection/bronchitis	4.9	337/6860
Diarrhoea/dysentery/AGE/loose motion	4.7	321/6860
Mental problem/anxiety/SOB/depression	4.7	319/6860
APD/gastritis/peptic ulcer	3.1	216/6860
Headache/migraine/TTH	3.0	204/6860
Snake bite	2.9	202/6860
Other	49.2	3373/6860
Prescribing indicator		
Percentage of patients prescribed an antibiotic	44.7	3064/6860
Number of antibiotics prescribed[c]		
Uncertain or none	55.3	3796/6860
One antibiotic	35.7	2452/6860
Two antibiotics	8.4	578/6860
Three antibiotics	0.5	32/6860
Four antibiotics	0.03	2/6860

[a]n_j numerator; [b]n_k denominator; [c]denominator for calculation of percentages is number of patient records collected.

Note: ARI: Acute respiratory tract infection, URTI: Upper respiratory tract Infection, LRTI: Lower respiratory tract infection, AGE: Acute gastroenteritis, SOB: Shortness of breath, APD: Acid peptic disease, TTH: Tension-type headache.

The study was approved by the Human Research Ethics Committee, Curtin University (HRE2017-0394) and the ethics committee of the Nepal Health Research Council (Reg no.189/2017). Permission for collecting the required administrative information of patient from public health facilities was obtained from the District Public Health Office, Rupandehi, Nepal (2193/2016-17).

Data analysis

Data were entered into an Excel spreadsheet for cleaning. Nearly one-fifth of the records (18.6%) had no information about medicines prescribed or administered to patients. These records were classified as having 'uncertain or no prescription (none)'. Analysis was done using Statistical Package for Social Sciences (SPSS) software version 25 (IBM Analytics, Armonk, NY, USA).

The administrative records at public health facilities are populated using text fields. No additional records on provisional or final diagnoses are available, thus the recording of diagnosis in the administrative records was considered as a final diagnosis. Since the disease were often described based on symptoms, similar symptoms or conditions were grouped together.

Antibiotics were defined as antibacterial agents, including metronidazole, irrespective of formulation. A core prescribing indicator, "*the percentage of patients prescribed an antibiotic*" was computed in line with the WHO rational drug use methodology [34]. Antibiotics were grouped into classes based on the antibiotic's chemical structure or chemical class [35]. Frequency distributions of these classes were presented based on type of health facility.

Chi square tests were performed to examine the association between the prescribing of antibiotics for selected disease and conditions and explanatory variables including sex, age group, and type and department of health facility. Logistic regression was also used to examine factors associated with antibiotic prescribing for selected disease and conditions [36]. Selected disease and conditions included common ones for which a high number of antibiotics were prescribed, disease and conditions commonly needing antibiotics, and disease and conditions for which antibiotics are not expected to be prescribed for treatment. The significance level (α) was set at 0.05 for all statistical tests.

Results

Patient characteristics and prescribing indicators

In total 6,860 patient records were collected, with 1,278 (18.6%) records not having any information with regard to medicines, whether a prescribed or other medicine. Of these records, 5,582 (81.4%) had a record of medicines prescribed. Fifty-nine percent of patients were female. The highest number of records was for hospital emergency department presentations (29.9%) and hospital ambulatory visits (28.1%) with similar numbers for health post attendances (15.5%), primary health centre visits (13.8%) and hospital inpatient admissions (12.6%) (Table 1).

The most common presenting condition was pyrexia (9.9%). At least one antibiotic was prescribed in 3064 (44.7%) patient encounters, with more than one-third of patients (35.7%) prescribed one antibiotic and almost one in ten patients (8.9%) prescribed two or more antibiotics.

Antibiotic prescribing practices

Third-generation cephalosporins (29.9%) were the most commonly prescribed class of antibiotic, followed by penicillins (24.9%), quinolones (15.0%) and antiprotozoals (13.0%) (Table 2). Among antibiotics, the most commonly prescribed were ceftriaxone (22.9%), amoxicillin (16.6%), metronidazole (12.5%), ciprofloxacin (11.4%) and cotrimoxazole (7.2%).

Antibiotic prescribing was highest for hospital inpatients (64.6%) and lowest for hospital ambulatory (29.7%), with approximately half of patients visiting health posts (52.2%) and primary health care centres (50.4%) prescribed an antibiotic (Table 3). Conditions for which the antibiotic prescribing rate was highest included pneumonia (85.5%), diarrhoea and related conditions (83.2%), respiratory infections (72.4%), chronic obstructive pulmonary disease (COPD) (68.4%), pyrexia (66.1%), colds, sinusitis and rhinitis (65.3%), snake bites (64.4%) and coughs (63.1%).

The class of antibiotics prescribed varied by health facility and department. Third-generation cephalosporins were the most common antibiotics prescribed for patients presenting at emergency departments and hospital inpatients (56.8% and 49.2%, respectively), whereas penicillins (46.5%) and quinolones (23.1%) were most commonly prescribed in primary health centres. In health posts, prescribing rates of sulfonamides (28.8%), penicillins (26.0%) and quinolones (21.1%) were almost similar.

Third-generation cephalosporins were the most commonly prescribed antibiotic for the treatment of pneumonia (28.6%), COPD (41.0%), fever (40.2%),

snake bite (88.6%) and abdominal pain including nausea, vomiting and dyspepsia (62.2%). Penicillins were also often prescribed for the treatment of pneumonia (27.0%) and were the most commonly used antibiotic for respiratory tract infections (43.9%), common colds (41.4%), coughs (48.6%), skin infections (56.2%), and falls and injuries (71.5%). For skin diseases and diarrhoeal cases, sulfoanmides (41.9%) and antiprotozals (57.6%) were the most commonly prescribed antibiotics respectively.

Factors associated with antibiotic prescribing for selected disease and conditions

Across all disease and conditions, antibiotic prescribing was significantly associated with sex, age group and type of facility/department (Table 4). Males were more likely to receive antibiotics than females ($p = 0.005$), patients less than 5 years were more likely than all other age groups to receive antibiotics ($p < 0.001$) and inpatients were more likely to receive antibiotics than other hospital patients and those attending primary health care facilities and health posts ($p < 0.001$).

Factors associated with antibiotic prescribing varied by condition (Supplementary Tables 1-4). The only condition for which the antibiotic prescribing rate differed between males and females was common colds, with males less likely to be prescribed antibiotics than females ($p = 0.023$).

Antibiotic prescribing was significantly associated with age group for several conditions. Older age groups were less likely than children less than 15 years old to receive antibiotics for skin infections ($p < 0.05$), respiratory infections ($p < 0.05$) and skin diseases ($p < 0.01$). Similarly, younger patients were less likely to receive antibiotics for diarrhoea ($p = 0.015$) and COPD ($p = 0.001$). In contrast, patients aged 45 years and above age were less likely to receive antibiotics for snake bite than those less than 25 years old ($p < 0.05$).

Table 2. Commonly prescribed antibiotics by class and name.

SN	Prescribed antibiotic's name and classes	Total no	Total share (%)	Total share within class (%)	Total share (%)
1	**Penicillins**	**926**	**24.9**		
	Amoxicillin	618		66.7	16.6
	Ampicillin	112		12.1	3.0
	Cloxacillin	65		7.0	1.8
	Amoxicillin Clavulanate	35		3.8	0.9
	Other	96		10.4	2.6
2	**Tetracyclines**	**58**	**1.6**		
	Doxycycline	47		81.0	1.3
	Other	11		19.0	0.3
3	**Cephalosporins**	**1111**	**29.9**		
	Ceftriaxone	851		76.6	22.9
	Cefixime	143		12.9	3.9
	Cefpodoxime	60		5.4	1.6
	Other	57		5.1	1.5
4	**Quinolones**	**557**	**15.0**		
	Ciprofloxacin	424		76.1	11.4
	Levofloxacin	120		21.5	3.2
	Other	13		2.3	0.4
5	**Macrolides**	**171**	**4.6**		
	Azithromycin	163		95.3	4.4
	Other	8		4.7	0.2
6	**Sulfonamides**	**267**	**7.2**		
	Cotrimoxazole	267		100.0	7.2
	Other	0		0.0	0.0
7	**Antiprotozoal**	**484**	**13.0**		
	Metronidazole	465		96.1	12.5
	Other	19		3.9	0.5
8	**Others**	**138**	**3.7**		
	Amikacin	62		45.3	1.7
	Fluconazole	49		35.8	1.3
	Other	27		19.0	0.7
	Total	**3712**	100.0		100.0

Table 3. Descriptive analysis of prescriptions and prescribed classes of antibiotic by types and department of health facility and selected diseases and conditions.

Variables	Antibiotic prescribed (n=6860)		Classes of antibiotic prescribed (%) (n = 3712)							
	Yes, n (%)	Uncertain or none, n (%)	Penicillins	Tetracyclines	Cephalosporins	Quinolones	Macrolides	Sulfonamides	Antiprotozoal	Others
Types and department of health facility										
All	3064 (44.7)	3796 (52.2)	24.9	1.6	29.9	15.0	4.6	7.2	13.0	3.7
Inpatient hospital	559 (64.6)	306 (35.4)	14.0	1.1	49.2	13.4	1.9	0.0	12.8	7.6
Ambulatory hospital	572 (29.7)	1365 (70.3)	46.5	0.8	10.0	14.2	8.9	5.2	11.4	3.2
Emergency hospital	898 (43.8)	1154 (56.2)	15.9	0.0	56.8	9.5	2.2	0.0	13.7	2.0
Primary Health Centre	479 (50.4)	471 (49.6)	33.8	1.3	1.1	23.1	10.2	12.0	15.5	3.1
Health Post	556 (52.2)	509 (47.8)	26.0	6.3	0.2	21.1	3.3	28.8	11.6	2.7
Selected disease and conditions										
Pneumonia	46 (85.5)	6 (11.5)	27.0	0.0	28.6	14.3	6.3	15.9	1.6	6.3
Diarrhoea/dysentery/AGE/loose motion	267 (83.2)	54 (16.8)	1.7	1.2	20.0	16.5	0.5	2.2	57.6	0.2
ARI/URTI/LRTI/respiratory infection/ chest infection/bronchitis	244 (72.4)	93 (27.6)	43.9	2.7	9.8	8.2	14.5	19.2	0.8	0.8
COPD	128 (68.4)	59 (31.6)	19.7	1.1	41.0	24.2	9.0	2.2	2.2	0.6
Fever/pyrexia/PUO/FUO	450 (66.1)	231 (33.9)	23.7	1.1	40.2	19.4	4.3	2.4	3.7	5.0
Common cold/sinusitis/rhinitis	66 (65.3)	35 (34.7)	41.4	5.7	1.4	7.1	8.6	31.4	4.3	0.0
Snake bite	130 (64.4)	72 (35.6)	11.4	0.0	88.6	0.0	0.0	0.0	0.0	0.0
Cough/dry cough/allergic cough	99 (63.1)	58 (36.9)	48.6	1.8	5.5	9.2	21.1	11.9	0.0	1.8
Cellulitis/boils/impetigo/dermatitis/wound/skin infection/abscess	201 (48.7)	212 (51.3)	56.2	0.5	2.4	7.1	3.3	25.2	2.4	2.9
Falls and injury/injury/cut injury	157 (38.7)	249 (61.3)	71.5	0.0	16.3	4.7	1.2	4.7	1.7	0.0
Abdominal pain/nausea/ vomiting/dyspepsia	143 (36.9)	245 (63.1)	1.6	0.5	62.2	5.9	1.6	0.0	28.1	0.0
Skin diseases/skin allergy/sunburn/allergy/itching	59 (30.7)	133 (69.3)	37.1	3.2	3.2	4.8	6.5	41.9	3.2	0.0
Other	1074 (31.4)	2349 (68.6)	19.7	2.1	31.8	19.6	3.3	4.5	12.0	7.1

AGE: Acute Gastroenteritis, ARI: Acute Respiratory Tract Infection, URTI: Upper Respiratory Tract Infection, LRTI: Lower Respiratory Tract Infection, COPD: Chronic Obstructive Pulmonary Disease, PUO: Pyrexia of Unknown Origin, FUO: Fever of Unknown Origin.

Antibiotic prescribing was also significantly associated with type of health facilities. Patients attending health posts and health centre were more likely to receive antibiotics for respiratory infections (p = 0.007) and coughs (p = 0.002) than those attending hospitals. On the other hand, patient attending health posts and health centre were less likely to receive antibiotics for fever (p = 0.025) and COPD (p = 0.024). Patients presenting at emergency department with snake bites were more likely to receive antibiotics than patients admitted to the hospitals (p < 0.001).

Discussion

Antibiotic prescribing and associated factors

The percentage of patients prescribed at least one antibiotic (44.7%) was approximately twice the WHO recommended value of 20.0 to 26.8% [11,12]. The antibiotic prescribing rate for inpatients (64.6%) was higher than for patients in other facilities. This would be expected given the relative severity of illness of inpatients. In primary health care centres and health posts approximately half of medicines prescribed were antibiotics, possibly indicating excessive and inappropriate prescribing of antibiotics. These facilities often lack laboratory services and can be run single-handedly by a health worker who, although untrained, is expected to provide the full spectrum of services [26]. While other studies have tended not to cover all types of public health facilities, our findings on antibiotic prescribing rates in specific health care settings are consistent with several other studies in low- and middle-income countries [36-39].

Despite female attendance in public health facilities being higher than male attendance, consistent with reports of Nepal's Ministry of Health and Population [40], females were less likely to be prescribed antibiotics than males. This contrasts with the findings of a systematic review conducted in 10 high-income countries, which found females to be more likely to receive antibiotics [41]. Being a younger age increased the possibility of an antibiotic being prescribed in our study, although this varied by disease and conditions. Younger patients visiting a public health facility for skin infection, respiratory infection, skin disease and snakebite were more likely to be prescribed an antibiotic than older patients. A reason for higher antibiotic prescribing for children may be because children tend to get more infections [42]. Also infectious diseases are the leading cause of child mortality in many developing countries [43], and this may influence prescribing decisions to err on the side of caution when unsure of the underlining cause of symptoms.

Findings in our study of high prescribing rates of antibiotics for selected diseases such as diarrhoeal cases and respiratory infections suggested possible overprescribing and appear contrary to international recommendations. The WHO guidelines recommend oral rehydration solution with other supplements for

Table 4. Factors associated with antibiotic prescribing (n=6860).

Variables	Antibiotic prescribing			Univariable analysis			Multiple logistic regression	
	Yes, n (%)	Uncertain or none, n (%)	χ^2 (p value)	n	OR (95% CI)	p value	OR (95% CI)	p value
Gender								
Male	1346 (47.5)	1487 (52.5)	15.753 **(< 0.001)**	2833	1	**< 0.001**	1	**0.005**
Female	1718 (42.7)	2308 (57.3)		4026	0.822 (0.747, 0.906)		0.863 (0.779, 0.956)	
Age group								
Less than 5 years	251 (69.7)	109 (30.3)	183.883 **(< 0.001)**	360	1		1	
5 to 14 years	538 (54.2)	454 (45.8)		992	0.515 (0.398, 0.666)	**< 0.001**	0.568 (0.435, 0.740)	**< 0.001**
15 to 24 years	549 (39.9)	827 (60.1)		1376	0.288 (0.225, 0.370)	**< 0.001**	0.293 (0.227, 0.379)	**< 0.001**
25 to 44 years	791 (38.6)	1259 (61.4)		2050	0.273 (0.214, 0.347)	**< 0.001**	0.298 (0.232, 0.382)	**< 0.001**
45 to 64 years	537 (41.9)	745 (58.1)		1282	0.313 (0.244, 0.402)	**< 0.001**	0.328 (0.253, 0.425)	**< 0.001**
65 and above	398 (49.8)	402 (50.3)		800	0.430 (0.330, 0.560)	**< 0.001**	0.481 (0.366, 0.631)	**< 0.001**
Type and department of health facility								
Inpatient hospital	559 (64.4)	306 (35.4)	352.791 **(< 0.001)**	865	1		1	
Ambulatory hospital	572 (29.7)	1356 (70.3)		1928	0.231 (0.195, 0.274)	**< 0.001**	0.218 (0.183, 0.259)	**< 0.001**
Emergency hospital	898 (43.8)	1154 (56.2)		2052	0.426 (0.361, 0.502)	**< 0.001**	0.416 (0.352, 0.492)	**< 0.001**
Primary Health Centre	479 (50.4)	471 (49.6)		950	0.557 (0.461, 0.672)	**< 0.001**	0.507 (0.417, 0.615)	**< 0.001**
Health Post	556 (52.2)	509 (47.8)		1065	0.598 (0.497, 0.719)	**< 0.001**	0.582 (0.482, 0.703)	**< 0.001**

OR: Odds ratio; CI: Confident intervals.

non-bloody diarrhoea [44] and home care without antibiotics for children with respiratory symptoms [45].

Antibiotics usage patterns

Third-generation cephalosporins, penicillins and quinolones were the most frequently prescribed antibiotic classes, similar to findings of studies conducted in Pakistan [12], Saudi Arabia [46], Turkey [47] and Jordan [48]. Many hospitals in high-income countries also use large amounts of the cephalosporin class of antibiotics across a wide variety of infections. Their undoubted popularity relies upon lesser allergenic and toxicity risks as well as a broad spectrum of activity [49], although guidelines including in Nepal do not recommend cephalosporins as a first-line treatment for some indications [18]. Guidelines advise that cephalosporins should be avoided as a first-line treatment, when a narrower spectrum antibiotic would be effective because they increase the risk of *Clostridioides difficile*, methicillin-resistant *Staphylococcus aureus* (MRSA) and other resistant infections [49,50]. Countries, and even individual hospitals, where cephalasporins are used more often have been shown to experience higher rates of multidrug resistant organisms, although determining if these rates result from the higher use specifically of cephalosporin antibiotics rather than all antibiotic classes is difficult [49].

Policy implications

Levels of antibiotic prescribing above the WHO recommended rate suggest the need to implement measures to reduce potential overprescribing. Diagnostic uncertainty is a likely factor contributing to the high prescribing rate of antibiotics, particularly at primary health care centres and health posts. Almost half of primary health care centres in Nepal do not have physicians or laboratory technicians [26], and initiatives to fill these positions could improve prescribing practices. The patient-provider relationship may also impact on prescribing [51]. The expectation of patient is also a crucial factor for antibiotic prescribing and providers often prescribe antibiotics to meet their expectation [52]. With primary health care centres mostly located in the villages and these populations geographically isolated [53], few other options for treatment are available. Providers and community members are known to each other and providers may be under pressure to prescribe antibiotics [39,51,54]. A targeted intervention to provide education and training to physicians and health workers about antimicrobial resistance and prescribing antibiotics only when they are necessary, together with initiatives to monitor antimicrobial prescribing, could promote more appropriate prescribing behaviours.

Additionally, the relatively high prescribing rate of third-generation cephalosporins and quinolones in public facilities in Nepal is of concern, given that third-generation cephalosporins and quinolones are considered second-line antibiotics in most guidelines. When antibiotic therapy is necessary, the use of narrow-spectrum antibiotics should be used as first-line treatment whenever possible [55] to avoid drug-resistant bacteria developing. Therefore, any educational interventions to reduce inappropriate prescribing of antibiotics in unwarranted situations should also include education and training on the proper selection of antibiotics.

Strength and limitations

A strength of this study was the collection of data relating to antibiotic use across all levels of public health facilities, including hospitals, primary health care centres and health posts. At hospitals, data were separately collected for inpatients, patients attending ambulatory care clinics and those presenting at emergency departments. This enabled comparisons to be made across different levels of the public health system, and provides baseline evidence against which initiatives to improve antibiotic prescribing practices can be monitored. However, the study has several limitations. Almost one-fifth of records had no prescription information, and a medicine may have been prescribed but not recoded or a medicine may not have been prescribed at all. These cases were recorded as 'uncertain or no prescription'. Also many recorded diagnoses were non-specific, and coded as symptoms. These cases were grouped into broad categories together with related conditions. Having such broad categories made it difficult to assess appropriate use of antibiotics. It also prevented any investigation of whether antibiotic prescribing followed the standard guidelines.

Conclusion

Current patterns of antibiotic use in public health facilities in Nepal, especially in primary health care facilities, were found to be high compared with WHO guidelines. To prevent overuse and misuse of antibiotics, antimicrobial stewardship programmes should be adopted in public health facilities in Nepal. Given the lack of data on antibiotic use in public health facilities in Nepal, the information gained from this study will help in formulating policies and guidelines to

improve antibiotic use in public health facilities and limit the spread of antibiotic resistance. The findings may also be applicable to other low- and middle-income countries where the health system is similar to Nepal.

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Author contributions

Anant Nepal (AN) designed the study with input from Delia Hendrie (DH), Suzanne Robinson (SR) and Linda Selvey (LS). AN conducted the research including the analysis. DH conducted the coding check. AN drafted the manuscript and DH edited the manuscripts. All authors contributed to revisions and approved the final manuscript.

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Supplementary Table 1. Factors associated with antibiotic prescribing for selected diseases and conditions.

Variables	Diarrhoea (n = 321)						Falls and injuries (n = 406)						Abdominal pain (n = 388)					
	Univariable analysis			Multiple logistic regression			Univariable analysis			Multiple logistic regression			Univariable analysis			Multiple logistic regression		
	Yes, n (%)	Uncertain or none, n (%)	χ^2 (p value)	n	OR (95% CI)	p value	Yes, n (%)	Uncertain or none, n (%)	χ^2 (p value)	n	OR (95% CI)	p value	Yes, n (%)	Uncertain or none, n (%)	χ^2 (p value)	n	OR (95% CI)	p value
Gender																		
Male	103 (78.6)	28 (21.4)	3.277 (0.070)	131	0.700 (0.379, 1.292)	0.254	101 (40.9)	146 (59.1)	1.312 (0.252)	247	1	0.223	67 (38.7)	106 (61.3)	0.470 (0.493)	173	1	0.372
Female	164 (86.3)	26 (13.7)		190	1		56 (35.2)	103 (64.8)		159	0.772 (0.509, 1.170)		76 (35.3)	139 (64.7)		215	0.823 (0.536, 1.263)	
Age group																		
Less than 15 years	50 (68.5)	23 (31.5)	16.140 **(< 0.001)**	73	0.398 (0.189, 0.837)	**0.015**	42 (36.5)	73 (63.5)	1.481 (0.477)	115	0.699 (0.403, 1.212)	0.202	20 (32.3)	42 (67.7)	2.590 (0.274)	62	1	0.276
15 to 44 years	134 (89.9)	15 (10.1)		149	1.573 (0.730, 3.390)	0.247	70 (37.2)	118 (62.8)		188	0.739 (0.451, 1.210)	0.229	93 (40.1)	139 (59.9)		232	1.407 (0.761, 2.601)	
45 and above	83 (83.8)	16 (16.2)		99	1		45 (43.7)	58 (56.3)		103	1		30 (31.9)	64 (68.1)		94	0.910 (0.451, 1.836)	0.792
Type of health facilities																		
All hospital	170 (82.5)	36 (17.5)	0.175 (0.675)	206	0.754 (0.395, 1.440)	0.392	133 (37.6)	221 (62.4)	1.408 (0.235)	354	0.689 (0.381, 1.246)	0.218	134 (38.3)	216 (61.7)	3.140 (0.076)	350	1	0.077
Health post and health centre	97 (82.1)	18 (17.9)		115	1		24 (46.2)	28 (53.8)		52	1		9 (23.7)	29 (76.3)		38	0.490 (0.222, 1.081)	

OR: Odds ratio; CI: Confident intervals. Note: The following different conditions had included in the group for analysis: **Diarrhoea**: Diarrhoea/dysentery/AGE/loose motion; **Fall and Injuries**: Falls and injury/injury/cut injury; **Abdominal pain**: Abdominal pain/nausea/vomiting/dyspepsia.

Supplementary Table 2. Factors associated with antibiotic prescribing for selected diseases and conditions.

Variables	Skin Infection (n = 413)						Fever (n = 681)						ARI (n = 337)					
	Univariable analysis			Multiple logistic regression			Univariable analysis			Multiple logistic regression			Univariable analysis			Multiple logistic regression		
	Yes, n (%)	Uncertain or none, n (%)	χ^2 (p value)	n	OR (95% CI)	p value	Yes, n (%)	Uncertain or none, n (%)	χ^2 (p value)	n	OR (95% CI)	p value	Yes, n (%)	Uncertain or none, n (%)	χ^2 (p value)	n	OR (95% CI)	p value
Gender																		
Male	107 (50.7)	104 (49.3)	0.720 (0.396)	211	1	0.530	212 (66.5)	107 (33.5)	0.038 (0.845)	319	0.992 (0.718, 1.369)	0.959	121 (74.2)	42 (25.8)	0.529 (0.467)	163	1	0.494
Female	94 (46.5)	108 (53.5)		202	0.881 (0.593, 1.308)		238 (65.7)	124 (34.3)		362	1		123 (70.7)	51 (29.3)		174	0.841 (0.512, 1.381)	
Age group																		
Less than 15 years	111 (58.7)	78 (41.3)	15.321 **(< 0.001)**	189	1	**< 0.001**	176 (69.3)	78 (30.7)	2.150 (0.341)	254	1	0.135	83 (82.2)	18 (17.8)	7.476 **(0.024)**	101	1	**0.009**
15 to 44 years	56 (37.6)	93 (62.4)		149	0.428 (0.275, 0.665)		163 (63.2)	95 (36.8)		258	0.753 (0.519, 1.092)		95 (66.4)	48 (33.6)		143	0.437 (0.233, 0.817)	
45 and above	34 (45.3)	41 (54.7)		75	0.586 (0.342, 1.005)	0.052	111 (65.7)	58 (34.3)		169	0.828 (0.546, 1.258)	0.377	66 (71.0)	27 (29.0)		93	0.464 (0.231, 0.930)	**0.030**
Type of health facilities																		
All hospital	100 (50.3)	99 (49.7)	0.385 (0.535)	199	1	0.766	338 (68.6)	155 (31.4)	4.902 **(0.027)**	493	1	**0.025**	91 (65.0)	49 (35.0)	6.570 **(0.010)**	140	0.503 (0.304, 0.830)	**0.007**
Health post and health centre	101 (47.2)	113 (52.8)		214	0.942 (0.634, 1.399)		112 (59.6)	76 (40.4)		188	0.671 (0.473, 0.951)		153 (77.7)	44 (22.3)		197	1	

OR: Odds ratio; CI: Confident intervals. Note: The following different conditions had included in the group for analysis: **Skin infection:** Cellulitis/boils/impetigo/dermatitis/wound/skin infection/abscess; **Fever:** Fever/pyrexia/PUO/FUO; **ARI**: ARI/URTI/LRTI/respiratory infection/chest infection/bronchitis.

Supplementary Table 3. Factors associated with antibiotic prescribing for selected diseases and conditions.

Variables	Cough (n = 157)						Skin diseases (n=192)						Common cold (n=101)					
	Univariable analysis			Multiple logistic regression			Univariable analysis			Multiple logistic regression			Univariable analysis			Multiple logistic regression		
	Yes, n (%)	Uncertain or none, n (%)	χ^2 (p value)	n	OR (95% CI)	p value	Yes, n (%)	Uncertain or none, n (%)	χ^2 (p value)	n	OR (95% CI)	p value	Yes, n (%)	Uncertain or none, n (%)	χ^2 (p value)	n	OR (95% CI)	p value
Gender																		
Male	39 (57.4)	29 (42.6)	1.676 (0.196)	68	0.592 (0.295, 1.189)	0.141	23 (29.5)	55 (70.5)	0.095 (0.758)	78	1	0.895	16 (50.0)	16 (50.0)	4.872 **(0.027)**	32	0.332 (0.128, 0.860)	**0.023**
Female	60 (67.4)	29 (32.6)		89	1		36 (31.6)	78 (68.4)		114	0.955 (0.482, 1.893)		50 (72.5)	19 (27.5)		69	1	
Age group																		
Less than 5 years 5 to 14 years 15 to 24 years	22 (71.0)	9 (29.0)		31	1		32 (56.1)	25 (43.9)		57	1		28 (73.7)	10 (26.3)		38	1	
25 to 44 years	41 (61.2)	26 (38.8)	1.038 (0.595)	67	0.507 (0.190, 1.351)	0.174	17 (19.3)	71 (80.7)	24.647 **(< 0.001)**	88	0.182 (0.086, 0.386)	**< 0.001**	25 (61.0)	16 (39.0)	1.893 (0.388)	41	0.415 (0.145, 1.182)	0.100
45 to 64 years 65 and above	36 (61.0)	23 (39.0)		59	0.536 (0.200, 1.435)	0.215	10 (21.3)	37 (78.7)		47	0.203 (0.083, 0.498)	**< 0.001**	13 (59.1)	9 (40.9)		22	0.491 (0.151, 1.594)	0.237
Type of health facilities																		
All hospital	41 (51.2)	39 (48.8)	9.762 (0.002)	80	0.335 (0.168, 0.667)	**0.002**	18 (30.5)	41 (69.5)	0.002 (0.965)	59	1	0.581	9 (50.0)	9 (50.0)	2.278 (0.131)	18	0.600 (0.199, 1.803)	0.363
Health post and health centre	58 (75.3)	19 (24.7)		77	1		41 (30.8)	92 (69.2)		133	0.817 (0.398, 1.676)		57 (68.7)	26 (31.3)		83	1	

OR: Odds ratio; CI: Confident intervals. Note: The following different conditions had included in the group for analysis: **Cough:** Cough/dry cough/allergic cough; **Skin diseases:** Skin diseases/skin allergy/sunburn/allergy/itching; **Common cold:** Common cold/sinusitis/rhinitis.

Supplementary Table 4. Factors associated with antibiotic prescribing for selected diseases and conditions.

Variables	COPD (n = 187)						Variables	Snakebite (n = 202)					
	Univariable analysis			Multiple logistic regression				Univariable analysis			Multiple logistic regression		
	Yes, n (%)	Uncertain or none, n (%)	χ^2 (p value)	n	OR (95% CI)	p value		Yes, n (%)	Uncertain or none, n (%)	χ^2 (p value)	n	OR (95% CI)	p value
Gender									**Gender**				
Male	58 (73.4)	21 (26.6)	1.564 (0.211)	79	1	0.209	Male	53 (68.8)	24 (31.2)	1.086 (0.297)	77	1	0.193
Female	70 (64.8)	38 (35.2)		108	0.646 (0.327, 1.276)		Female	77 (61.6)	48 (38.4)		125	0.644 (0.331, 1.250)	
Age group									**Age group**				
Less than 65 years	39 (51.3)	37 (48.7)	17.404 **(< 0.001)**	76	0.287 (0.147, 0.559)	**< 0.001**	Less than 25 years	62 (68.9)	28 (31.1)	4.109 (0.128)	90	1	0.647
65 and above	89 (80.2)	22 (19.8)		111	1		25 to 44 years	50 (65.8)	26 (34.2)		76	0.848 (0.419, 1.718)	
Type of health facilities							45 and above	18 (50.0)	18 (50.0)		36	0.399 (0.170, 0.935)	**0.035**
All hospital	116 (73.0)	43 (27.0)	9.987 **(0.002)**	159	1	**0.024**			**Type and department**				
Health post and health centre	12 (42.9)	16 (57.1)		28	0.366 (0.153, 0.877)		Hospital Inpatient	25 (39.1)	39 (60.9)	26.128 **(< 0.001)**	64	0.191 (0.100, 0.367)	**< 0.001**
							Hospital Emergency	105 (76.1)	33 (23.9)		138	1	

OR: Odds ratio; CI: Confident intervals.