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Antibiotic dispensing practices in private pharmacies in Nepal

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Abstract

Objectives: Private pharmacies are widely established in most low- and middle-income countries (LMICs) including Nepal, and are often considered as a patient's first point of contact for seeking healthcare. The aim of this study was to investigate patterns of antibiotic dispensing practices at private pharmacies through exit interviews with patients by reviewing their medication information.

Design and setting: Cross-sectional study. Data collection was carried out in 60 days at 33 randomly selected private pharmacies in the Rupandehi district of Nepal

Participants: Patients attending private pharmacies (n=1537)

Main outcome measure: Patterns of antibiotic prescribing and dispensing were investigated using WHO's core prescribing indicator, "*the percentage of patients prescribed an antibiotic*". Frequency distributions were presented based on patients' characteristics, registration status of pharmacies and education of the pharmacists or drug retailer, dispensing practice and disease or conditions. Chi-square tests and regression analysis were applied to explore factors associated with antibiotic dispensing practices.

Results: Of patients attending private pharmacies, the proportion receiving at least one antibiotic (38.4%) was above the WHO recommended value (20.0 to 26.8%). The most commonly dispensed antibiotics were cefixime (16.9%) and the third generation cephalosporins (38.0%) class. High dispensing rates of antibiotics for selected conditions (e.g. respiratory infections, diarrhoeal cases) appeared contrary to international recommendations. The percentage of antibiotic dispensed was highest for patients who obtained their medicines from unlicensed pharmacies (59.1%). Young people were more likely to receive antibiotics than other age groups.

Conclusions: Antibiotic dispensing patterns from private pharmacists in Nepal was high compared with WHO guidelines, suggesting initiatives to reduce inappropriate use of antibiotics should be implemented. The findings of this study may be generalisable to other LMICs in order to develop policies and guidelines to promote more appropriate dispensing and prescribing practices of antibiotics and limit the spread of antibiotic resistance.

Strength and limitation of this study

- The study provides an evidence base about current dispensing practices from private pharmacies and a baseline against which to measure the effectiveness of future policies and programmes to reduce the level of inappropriate dispensing of antibiotics.
- Data on dispensing of medications including antibiotic was sourced directly from patients and validated from the dispensed medicines.
- The findings reinforce calls to build a strong regulatory environment in advancing prudent antibiotic use, which may also be applicable to other low- and middle-income countries.
- The reporting of diagnoses or conditions by patients was more symptom-based so had to be grouped into broad categories together with related conditions.
- Grouping conditions into broad categories made it difficult to assess appropriate use of antibiotics and whether antibiotic dispending and prescribing followed the standard guidelines.

Introduction

The role of the private sector in health care in low- and middle-income (LMICs) countries has often been neglected by governments and international public health communities (1). However, private pharmacies and drug stores are widely established in most LMICs, and usually considered as a patient's first point of contact for healthcare and the preferred channel through which to get health services and medicines (2). These pharmacies range from high end outlets staffed by pharmacists to small, rural, road side stalls staffed by someone without formal health qualifications. Because of ease of access, more flexible opening hours, availability of cheaper medicines and credit (3) and personal intimacy (4), consumers often tend to utilise private rather than public facilities (5). Further, many patients have neither the time nor money to consult a physician (6) preferring over-the-counter medicines and healthcare advice. Globally, two thirds of all antibiotics are sold without prescription through unregulated private sector pharmacies or drug stores (7).

Non-prescription use of antibiotics is associated with the risk of inappropriate drug use, defined as patients not receiving the appropriate medicines in doses that meet their individual requirements, for an adequate duration, and at the lowest cost (7). Inappropriate use of medicines is a serious global problem occurring in both developed and developing countries (8), with the World Health Organization (WHO) estimating more than half of all medicines are inappropriately prescribed, dispensed, or sold (7). This overuse and misuse of antibiotics is one of the main causes of antibiotics becoming ineffective (9), thus posing problems relating to treatment failure and other costs to the individual and society (10-12).

In Nepal, dispensing of medicines is undertaken by pharmacists and drug retailers or sellers and many dispensers have admitted treating patients too by also prescribing medicines (13). Pharmacists have three to five years of pharmacy education (13), however, drug retailers and sellers include individuals who are only associated with private pharmacies, do not necessarily have formal education in dispensing medicines, but can undertake training and obtain a licence to own and operate a pharmacy from the Department of Drug Administration (DDA), the government body dealing with medicines and their related affairs (14, 15). Practicing healthcare without a license is illegal in Nepal (16), however many unlicensed pharmacies are also operating in remote areas of Nepal (17). Little is known about the antibiotic dispensing practices from licensed or unlicensed private pharmacies in Nepal. Previous studies conducted in Nepal that have examined antibiotic dispensing practices from private pharmacies have collected data directly from pharmacists or drug sellers themselves (17, 18), which may result in inaccurate reporting of dispensing practices. This study has investigated patterns of antibiotics dispensing practices through exit interviews with patients by reviewing their medication information, thus ensuring collection of reliable information. The findings of this study reveal issues about inappropriate use of antibiotics and can be used as a baseline against which to evaluate initiatives to improve antibiotic dispensing and prescribing practices in the private pharmacy sector in Nepal.

Methods

The study was a cross-sectional study conducted in the Rupandehi district of Nepal. Private pharmacies were selected based on WHO guidelines (19, 20). Before selecting the private pharmacies, six survey areas were selected from the seven electoral areas in the district. 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. Altogether, six public health facilities were selected, two each from hospitals, primary healthcare centres and health posts, with the major hospital included as one of the hospitals (as per WHO guidelines). These health facilities used as the basis for selecting the private pharmacies.

Five private pharmacies were selected from each survey area from a list made available by the Nepal Chemists and Druggists Association, Lumbini, Nepal. Separate pharmacies and pharmacies attached to private hospitals were included in the sample to represent both types. This list was verified after visiting each selected survey area and updated by deleting any duplicate pharmacies and adding any missing from the records. Three private facilities from within five kilometres and two located greater than five kilometres from each public health facility were randomly selected. Three private pharmacies were added to the original sample due to refusal of the

initially selected pharmacies to allow data collection on the second day. Each pharmacy was surveyed for two days, other than the three that refused data to be collected on the second day and the three replacement pharmacies, which were surveyed for one day. Thus data collection covered 60 days (2 days per pharmacy for 27 pharmacies and 1 day per pharmacy for 6 pharmacies).

Data collection

Private pharmacies in Nepal do not follow the practice of keeping patients' records, so exit interviews were conducted with patients who had attended the selected pharmacies. Interviews were conducted from July 2017 to December 2017. The days allocated for data collection were based on the advice of pharmacists to obtain as representative a sample of days as possible. Interviews were conducted from 9.00 am to 5.00 pm and as many patients as possible who attended the selected pharmacies were included. Individuals obtaining medicines on behalf of another person were excluded from the exit interviews, however children attending the pharmacies with their parents or caretaker were included in the survey.

Data was collected using the Qualtrics Offline Surveys App (21). Demographic characteristics of the patients for whom the medicines had been bought (age, sex), the disease or condition and dispensing practice (self-medicated, recommended and supplied by a pharmacist without a prescription, or prescribed by a doctor and dispensed by a pharmacist) were collected. Photographs were taken of the medicines, with no patient identifiers included in the photos and attached to the App. The maximum time taken for the exit interview was three minutes. Prior to the interview, all consumers were informed of the nature of the study and written consent was sought to interviews being conducted. Consent for patients younger than 18 years was sought from the accompanying parent or caretaker.

The principal researcher (AN) coordinated data collection and approached respective authorities and health facilities to obtain approval to collect the data, and Nepali 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, the importance of ensuring 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 entered records in the Qualtrics App.

Data analysis

The data were imported from the Qualtrics App to MSExcel spreadsheet for cleaning. The cleaned data were transferred to SPSS statistical software (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: USA). Diseases or conditions collected from the interviews were generally described based on symptoms, thus similar symptoms were grouped together. For some analyses, the three most commonly occurring groups (i.e. fevers, respiratory symptoms and skin conditions) were separately analysed, with remaining groups combined into those likely to require antibiotics ("other - infectious"), and those not likely to require antibiotics ("other - non- infectious"). Antibiotics were also grouped into classes for analysis (22). A core prescribing indicator, "*the percentage of patients prescribed an antibiotic*" was computed in line with the WHO's rational drug use methodology (23-25). Descriptive analysis was conducted to show commonly dispensed antibiotics and antibiotic dispensing by dispensing practice, registration status of pharmacies and education of the pharmacist or drug retailer, and disease or condition. Chi square tests were performed to examine the association between antibiotic dispensing and explanatory variables including sex, age group, dispensing practices and registration status of pharmacies and education status of the pharmacist or drug retailer. Logistic regression was also used to examine factors associated with antibiotic dispensing. An interaction term of dispensing practices with registration status and education was also examined. The significance level (α) was set at 0.05 for all statistical tests.

Results

Characteristics of patients and prescription information

Of the 1,554 patients approached for an interview, 15 (1.0%) refused to participate, thus giving a sample size of 1537 patients. The sample comprised a similar number of male and female respondents, with all age groups relatively well represented (Table 1). Just over half of patients (55.2%) had a prescription from a doctor or health worker, with about one quarter not having a prescription but purchasing a medicine recommended and supplied by the pharmacist. Almost equal numbers of patients received their medicine from a pharmacist who had a diploma or bachelor's degree in pharmacy (49.6%) and those who had completed training from DDA (46.1%). The most commonly occurring diseases or conditions were fevers (18.1%), coughs (5.3%), and respiratory infection (4.9%). At least one antibiotic was dispensed in 947 (38.4%) patient encounters.

Table 1 Patient characteristics and information related to dispensing of medicines

Variables	Percentage	n_i/n_k [b,c]
Sex		
Male	50.5	776/1537
Female	49.5	761/1537
Age group of patient		
Less than 14 years	19.4	298/1537
15 to 24 years	20.2	310/1537
25 to 44 years	35.0	538/1537
45 and above years	25.4	391/1537
Dispensing practice		
Prescribed by a doctor or health worker and dispensed by a pharmacist	55.2	848/1537
Recommended and supplied by a pharmacist without a prescription	26.1	401/1537
Self-medicated	13.3	205/1537
Old prescription	5.4	83/1537
Registration status/education		
Licensed/diploma or bachelors in pharmacy	49.6	762/1537
Licensed/training from DDA	46.1	709/1537
Unlicensed/education unknown	4.3	66/1537
Diseases and conditions*		
Fever	18.1	278/1537
Cough	5.3	82/1537
Respiratory infection	4.9	75/1537
Headache	4.8	74/1537
Loss of appetite	4.7	72/1537
Skin infections	4.6	70/1537
Common cold	4.4	68/1537
Cut injuries	4.4	67/1537
Acid peptic diseases	4.3	66/1537
Body ache	4.2	65/1537
Heart disease	4.2	64/1537
Fungal infection	3.8	59/1537
Skin diseases	3.7	57/1537
Abdominal discomfort	3.6	55/1537
Arthritis and bone pain	3.3	50/1537
Others	21.8	335/1537
Prescribing indicator		
Percentage of patients dispensed an antibiotic	38.4	590/1537
No of antibiotics dispensed		
No antibiotic	61.6	947/1537
One antibiotic	35.8	551/1537
Two antibiotics	2.5	39/1537

[b] n_i *numerator*
[c] n_k *denominator*

DDA: Department of Drug Administration

***Diseases or conditions included:**
***Fever:** Fever and pyrexia
***Cough:** Cough, dry cough and allergic cough
***Respiratory infections:** Acute respiratory infection, respiratory infection, chest infection and bronchitis
***Loss of appetite:** Weakness, anorexia and loss of appetite
***Skin infections:** Boils, dermatitis, wound and skin infection
***Common cold:** Common cold and sinusitis
***Cut injuries:** Injuries and cut injuries
***Acid peptic diseases:** Acid peptic diseases, gastritis, peptic ulcer, and upper gastrointestinal bleeding
***Body ache:** Body ache and backache
***Heart disease:** Heart disease and hypertension
***Fungal infection:** Fungal infection and ring worm
***Skin diseases:** Skin diseases and skin allergy
***Abdominal discomfort:** Abdominal pain, nausea, vomiting and dyspepsia
***Arthritis and bone pain:** Arthritis, joint pain, leg Pain and shoulder Pain

Commonly dispensed antibiotic

Among antibiotics, the most commonly dispensed were cefixime (16.9%), amoxicillin (12.2%), cefpodoxime (10.3%), ampicillin+cloxacillin (8.7%) and then ciprofloxacin (8.7%). Cephalosporins (38.0%) were the most commonly dispensed class of antibiotics, followed by penicillins (29.3%), quinolones (13.7%) and then marcolides (8.1%) (Table 2).

Table 2 Commonly dispensed antibiotics

SN	Dispensed antibiotics	No	%
1	Cefixime	106	16.9
2	Amoxicillin	77	12.2
3	Cefpodoxime	65	10.3
4	Ampicillin+Cloxacillin	55	8.7
5	Ciprofloxacin	55	8.7
6	Azithromycin	49	7.8
7	Metronidazole	48	7.6
8	Amoxicillin+Clavulanate	31	4.9
9	Cefadroxil	16	2.5
10	Cephalexin	16	2.5
11	Levofloxacin	14	2.2
12	Ofloxacin	14	2.2
13	Amoxicillin+Cloxacillin	11	1.7
14	Cefixime + Clavulanic Acid	11	1.7
15	Other	61	9.7
	Total	**629**	**99.6**

SN	Dispensed antibiotic classes	No	%
1	Cephalosporins	239	38.0
2	Penicillins	184	29.3
3	Quinolones	86	13.7
4	Marcolides	51	8.1
5	Antiprotozoal	50	7.9
6	Others	19	3.0
	Total	**629**	**100**

The percentage of antibiotics dispensed was highest for those patients for whom the medicine had been prescribed by a doctor or health worker (58%). It was also highest for patients who obtained their medicines from an unlicensed pharmacy (59.1%). For several conditions, antibiotics were the most commonly dispensed medicine, including for respiratory infections (93.3%), diarrhoea and dysentery (91.3%), skin infections (87.1%), fever (70.5%) and urinary tract infection (57.9%).

The class of antibiotics dispensed was relatively similar by dispensing practice and registration status and education. Third generation Cephalosporins were the most common class of antibiotics recommended and supplied by a pharmacist or drug retailer without a prescription (40.7%) and prescribed by a doctor or health worker (38.1%), with Antiprotozoals the most common among patients who self-medicated (38.5%). Cephalosporins were also most commonly dispensed by both drug retailers who had training from DDA (41.3%) and those with a diploma or bachelors in pharmacy (36.1%). The highest dispensing rate of Cephalosporins was for the treatment of fever (69.5%), whereas penicillins were common for respiratory infections (60.8%), cut injuries (78.8%) and skin infections (67.2%) (Table 3).

Table 3 Descriptive analysis of dispensed classes of antibiotics by dispensing practice, registration status and education, and selected diseases and conditions

Variables	Antibiotics dispensed		Classes of antibiotics dispensed (%)					
	Yes = n (%)	No = n (%)	Cephalosporins = n (%)	Penicillins = n (%)	Quinolones = n (%)	Marcolides = n (%)	Antiprotozoal = n (%)	Others = n (%)
Dispensing practice								
Self-medicated	12 (4.2)	276 (95.8)	2 (15.4)	2 (15.4)	2 (15.4)	1 (7.7)	5 (38.5)	1 (7.7)
Recommended and supplied by a pharmacist without a prescription	86 (21.4)	315 (78.6)	35 (40.7)	14 (16.3)	12 (14.0)	8 (9.3)	14 (16.3)	3 (3.5)
Prescribed by a doctor or health worker and dispensed by a pharmacist	492 (58.0)	356 (42.0)	202 (38.1)	168 (31.7)	72 (13.6)	42 (7.9)	31 (5.8)	15 (2.8)
Registration status/education								
Licensed/diploma and bachelors in pharmacy	260 (34.1)	502 (65.9)	101 (36.1)	81 (28.9)	35 (12.5)	33 (11.8)	24 (8.6)	6 (2.1)
Licenced/training from DDA	291 (41.0)	418 (59.0)	128 (41.3)	90 (29.0)	39 (12.6)	16 (5.2)	26 (8.4)	11 (3.5)
Unlicensed/education unknown	39 (59.1)	27 (40.0)	10 (25.6)	13 (33.3)	12 (30.8)	2 (5.1)	0 (0.0)	2 (5.1)
Disease and condition*								
Respiratory infections	70 (93.3)	5 (6.7)	12 (16.2)	45 (60.8)	3 (4.1)	13 (17.6)	0 (0.0)	1 (1.4)
Diarrhoea and dysentery	42 (91.3)	4 (8.7)	4 (7.8)	0 (0.0)	10 (19.6)	0 (0.0)	37 (72.5)	0 (0.0)
Skin Infections	61 (87.1)	9 (12.9)	12 (19.7)	41 (67.2)	1 (1.6)	2 (3.3)	0 (0.0)	5 (8.2)
Fever	196 (70.5)	82 (29.5)	141 (69.5)	29 (14.3)	21 (10.3)	11 (5.4)	1 (0.5)	0 (0.0)
Urinary tract infection	22 (57.9)	16 (42.1)	1 (4.5)	0 (0.0)	18 (81.8)	0 (0.0)	0 (0.0)	3 (13.6)
Cut injuries	33 (49.3)	34 (50.7)	4 (12.1)	26 (78.8)	2 (6.1)	1 (3.0)	0 (0.0)	0 (0.0)
Common cold	16 (23.5)	52 (76.5)	6 (37.5)	5 (31.3)	1 (6.3)	4 (25.0)	0 (0.0)	0 (0.0)
Abdominal discomfort	10 (18.2)	45 (81.8)	3 (27.3)	0 (0.0)	4 (36.4)	0 (0.0)	4 (36.4)	0 (0.0)
Skin diseases	7 (12.3)	50 (87.7)	4 (57.1)	2 (28.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)
Cough	7 (8.5)	75 (91.5)	4 (40.0)	1 (10.0)	0 (0.0)	5 (50.0)	0 (0.0)	0 (0.0)
Other: infectious	104 (49.5)	106 (50.5)	38 (32.2)	29 (24.6)	23 (19.5)	14 (11.9)	6 (5.1)	8 (6.8)
Other: non-infectious	22 (4.5)	469 (95.5)	10 (43.5)	6 (26.1)	3 (13.0)	1 (4.3)	2 (8.7)	1 (4.3)

DDA: Department of Drug Administration

Diseases or conditions included:
Respiratory infections: *Acute respiratory infection, respiratory infection, chest infection and bronchitis*
Diarrhoea and dysentery: *Diarrhoea, dysentery and loose motion*

Skin infections: *Boils, dermatitis, wound and skin infection*
Fever: *Fever and pyrexia*
Cut injuries: *Injuries and cut injuries*
Common cold: *Common cold and sinusitis*
Abdominal discomfort: *Abdominal pain, nausea, vomiting and dyspepsia*
Skin diseases: *Skin diseases and skin allergy*
Cough: *Cough, dry cough and allergic cough*

Factors associated with antibiotic dispensing

Across all diseases and conditions, antibiotic dispensing was significantly associated with age group, prescription source, and registration status and education of pharmacists (Table 4). Patients less than 15 years were more likely than all other age groups to receive antibiotics (p=<0.001). Those patients who had a prescription from a doctor or health worker were also more likely to receive antibiotics than if patients had no prescription (p=<0.001). Similarly, patients were more likely to receive antibiotics from drug retailers who did not have a diploma or bachelors in pharmacy (p=0.001). The interaction term shows that the difference in patients receiving an antibiotic by registration status and education was greater if the medicine was prescribed by a doctor or health worker than when it was dispensed without a prescription.

Table 4 Factors associated with antibiotic dispensing

Variables	Antibiotics dispensing			Bivariable analysis			Multivariable analysis	
	Yes = n (%)	No = n (%)	X^2 (p-value)	n	OR (95% CI)	p-value	OR (95% CI)	p-value
Sex								
Male	302 (38.9)	474 (61.1)	0.187 (0.666)	776	1	0.666	1	0.576
Female	288 (37.8)	473 (62.2)		761	0.956 (0.778, 1.174)		0.934 (0.734, 1.188)	
Age group of patient								
Less than 15 years	177 (59.4)	121 (40.6)	98.876 (<0.001)	298	1		1	
15 to 24 years	116 (37.4)	194 (62.6)		310	0.409 (0.295, 0.566)	<0.001	0.464 (0.320, 0.672)	<0.001
25 to 44 years	210 (39.0)	328 (61.0)		538	0.438 (0.328, 0.584)	<0.001	0.432 (0.311, 0.602)	<0.001
45 and above years	87 (22.3)	304 (77.7)		391	0.196 (0.140, 0.273)	0.001	0.206 (0.142, 0.299)	<0.001
Dispensing practice								
Recommended and supplied by a pharmacist without a prescription (includes self-medication)	98 (14.2)	591 (85.8)	308.278 (<0.001)	689	0.120 (0.093, 0.155)	<0.001	0.087 (0.059, 0.128)	<0.001
Prescribed by a doctor or health worker and dispensed by a pharmacist	492 (58.0)	356 (42.0)		848	1		1	
Registration status and education								
Licensed/diploma and bachelors in pharmacy	260 (34.1)	502 (65.9)	11.627 (0.001)	762	0.698 (0.568, 0.859)	0.001	0.617 (0.465, 0.819)	0.001
Licensed/training from DDA (Includes unlicensed)	330 (42.6)	445 (57.4)		775	1		1	
Interaction term with dispensing practices, and registration status and education							1.987 (1.177, 3.354)	0.010

Discussion

In most developing countries, private pharmacies or drug stores are the first point of contact for people seeking healthcare (2). Antibiotics (and other prescription medicines) are readily available with or without prescription, and self-medication by patients is common. Non-prescription use of antibiotics is associated with a risk of inappropriate use due both to failure in dispensing in accordance with clinical guidelines and patients not using the drug appropriately (26). It is also one of the drivers of the emergence of antimicrobial resistance (27).

Findings of this study show the overuse of antibiotics dispensed from private pharmacies, with the percentage of patients dispensed an antibiotic (38%) being considerably higher than the level recommended by the WHO (38% versus 20 to 26.8%) (23, 24). This finding of overuse is consistent with studies conducted in private facilities in other LMICs including in India (28), Uganda (29) and Bangladesh (30).

Unlicensed pharmacies, especially outside of cities, often exist in low- and middle-income countries (31). These pharmacies sell medicines informally and are not legally recognised by the health system of the countries in which they operate (32). While, practicing healthcare without a license is illegal in Nepal (16), weak regulatory oversight of the Nepalese health system encourages pharmacies to operate without licences. This study found the level of dispensing of antibiotics was higher by unlicensed pharmacists. The education of operators of unlicensed pharmacies was unknown, and the perception is they are often minimally educated. It has been suggested in these circumstances that drug retailers may approach dispensing of medicines as any other sales job, not wanting a customer to leave without making a purchase (31). More generally, inappropriate dispensing of antibiotics may occur due to the business motive of private pharmacies with profits from antibiotics contributing to total profit (33).

Third generation cephalosporins was the most common antibiotic type recommended and dispensed with or without prescription. The finding is consistent with the studies conducted in India showing cephalosporins were the most commonly prescribed class of antibiotic in private pharmacies or clinics (28) and often used by urban private health facilities (34). Guidelines often 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 *Clostridium difficile, methicillin resistant Staphylococcus aureus (MRSA)* and other resistant infections (35, 36). Noticeably, third generation cephalosporins were dispensed to patients with minor symptoms, such as fever, which is self-limiting in most cases and could be a common symptom of several infections. The popularity of third generation cephalosporins lies in their lesser allergenic and toxicity risks as well as having a broad spectrum of activity (35). In Nepal treatment guidelines do not recommend cephalosporins as a first-line treatment for several infections such as respiratory tract infections, enteric fever, pneumonia and urinary tract infections (37).

Overprescribing and overuse of antibiotics in the treatment of respiratory infections and diarrhoea is a worldwide problem, potentially leading to widespread antimicrobial resistance (38). Contrary to international recommendations, this study found high prescribing rates of antibiotics for both conditions, suggesting possible overprescribing. The WHO guidelines recommend oral rehydration solution with other supplements for non-bloody diarrhoea (39) and home care without antibiotics for children with respiratory symptoms (40).

Across all conditions collectively, antibiotics were more likely to be dispensed to younger age groups especially less than 15 years of age compared to older groups. Respiratory diseases and diarrhoea impose a considerable health burden especially to children in LMICs (41, 42), and may lead to antibiotics being used more widely for the treatment of these diseases (43, 44). Higher self-medication practices among younger age groups could also be a factor contributing to higher antibiotic dispensing for younger age groups, with a study in Albania finding an association between self-medication and a higher use of antibiotics among younger age groups (45). Additionally increased education has been found to increase the risk of self-medication with antibiotics (46), and globally the literacy rates of young adults is higher than the elderly, with the differences is even wider in developing countries (47).

Policy implications

Levels of antibiotic prescribing above the WHO recommended rate suggests the need to implement measures to reduce potential inappropriate use in Nepal. Almost half of patients were dispensed antibiotics by drug retailers who, unlike pharmacists are professionally trained and do not have formal education in dispensing medicines. While this study did not examine their technical competencies, drug retailers should be encouraged to increase their skills through continued professional education.

In Nepal, the majority of health workers, who mostly work in public health facilities at the community level, have their own private pharmacies. Health workers are less qualified than medical doctors but are authorised to prescribe medicines as outlined in the antibiotic treatment guidelines (37). However, such guidelines are barely in practice or monitored (48). WHO's guideline of good pharmacy practices confines the role of pharmacists to dispensing only (49). A general lack of enforcement of the legislation covering registration of pharmacies and the distribution of antibiotics facilitates the inappropriate use of antibiotics in Nepal. Stronger enforcement mechanisms of pharmacy registration and restricting pharmacists and drug retailers supplying antibiotics without prescription should be established. Additionally, developing a national guidelines for good pharmacy practices and policy to reclassify antibiotics as special-control/prescription-only drugs in Nepal should be considered.

Private pharmacies are widely established in most LMICs including Nepal. They are usually considered as a patient's first point of contact and preferred channel to receive health services (2) particularly given issues relating to the unavailability and inaccessibility of quality of care from public health facilities (50). Private pharmacists and community members are often known to each other and pharmacists can be under pressure to prescribe antibiotics (51). Pharmacists and drug retailers generally do not charge consultation fees and profits from selling drugs is a main source of their income (52), which could encourage to sell antibiotics since it is one of the more profitable medicines (33). A targeted intervention to provide education and training relating to antimicrobial resistance and supplying antibiotics only with prescriptions will lead to greater consideration of antibiotic dispensing practices based on the standards of good pharmacy practices, thus contributing to a reduction in the risk of development of antibiotics resistance bacteria.

Additionally, the relatively high prescribing rate of third generation cephalosporins in private health facilities in Nepal is of concern, given that these classes 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 (53) to prevent drug-resistant bacteria developing. Educational interventions to reduce inappropriate dispensing or prescribing of antibiotics in unwarranted situations should include guidance on the proper selection of antibiotics.

Strength and limitations

Limited evidence is available in regard to antibiotic dispensing practices in LMICs. This study has provided an evidence base about current pharmacy dispensing practices in Nepal, with data on dispensing of medications including antibiotics sourced directly from patients and validated from the dispensed medicines. This information is useful in identifying ways that the dispensing of antibiotics is currently being practiced, and provides a baseline against which to measure the effectiveness of future policies and programmes to reduce the level of inappropriate dispensing of antibiotics. The findings of the study also reinforces calls to build a strong regulatory environment in advancing prudent antibiotic use. The findings may also be applicable to other low and middle income countries, where the health system is similar to Nepal.

However the study has several limitations. Diagnoses or conditions of patients were non-specific and recorded based on the understanding of the patients. Description of diagnoses or conditions were more symptom-based and 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 dispending and prescribing followed the standard guidelines. Another limitation is that Rupandehi district lies in a low-land region of Nepal, which has a greater availability of health services than in hill and high-hill regions. Results of the study are thus more generalisable to districts falling in low-land regions than hill and high-hill regions, a factor which needs to be considered in using findings from the study in developing and implementing policy to improve antibiotics pharmacy practice in Nepal.

Conclusion

This study documents antibiotic dispensing practices in private pharmacies in Nepal that were high compared with WHO guidelines. The unnecessary and inappropriate use of antibiotics has been associated with a higher prevalence of antimicrobial resistance (27). Given global concerns about antimicrobial resistance, evidence relating to overuse and misuse in a Nepal provides a rationale to consider introducing initiatives to reduce inappropriate use of antibiotics. Additionally this evidence may be more widely generalisable to other countries with similar health system financing arrangements.

Contributors 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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Data sharing statement The data used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval 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).

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STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Title: *Antibiotic dispensing practices in private pharmacies in Nepal*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any pre-specified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3 and 4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3 and 4
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	3 and 4
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	3 and 4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	3 and 4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	3 and 4
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	4
		(*b*) Describe any methods used to examine subgroups and interactions	4

		(*c*) Explain how missing data were addressed	4
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	3 and 4
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5 and 6
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	5 to 9
		(*b*) Report category boundaries when continuous variables were categorized	5 to 9
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10 and 11
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Survey of the pattern of antibiotic dispensing in private pharmacies in Nepal

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Survey of the pattern of antibiotic dispensing in private pharmacies in Nepal

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Abstract

Objectives: Private pharmacies are widely established in most low- and middle-income countries (LMICs) including Nepal, and are often considered as a patient's first point of contact for seeking healthcare. The aim of this study was to investigate the pattern of antibiotic dispensing in private pharmacies through exit interviews with patients to review their medication information.

Design and setting: Cross-sectional study. Data collection was carried out in 60 days at 33 randomly selected private pharmacies in the Rupandehi district of Nepal.

Participants: Patients attending private pharmacies (n=1537)

Main outcome measure: The pattern of antibiotic prescribing and dispensing was investigated using WHO's core prescribing indicator, "*the percentage of patients prescribed an antibiotic*". Frequency distributions were presented based on patients' characteristics, sources of antibiotic, registration status of pharmacies and education of the pharmacist or drug retailer, and disease or condition. Chi-square tests and regression analysis were applied to explore factors associated with the pattern of antibiotic dispensing.

Results: Of patients attending private pharmacies, the proportion receiving at least one antibiotic (38.4%) was above the WHO recommended value (20.0 to 26.8%). The most commonly dispensed antibiotics were cefixime (16.9%) and the third generation cephalosporins (38.0%) class. High dispensing rates of antibiotics for selected conditions (e.g. respiratory infections, diarrhoeal cases) appeared contrary to international recommendations. The percentage of antibiotic dispensed was highest for patients who obtained their medicines from unlicensed pharmacies (59.1%). Young people were more likely to receive antibiotics than other age groups.

Conclusions: Antibiotic dispensing pattern from private pharmacies in Nepal was high compared with WHO guidelines, suggesting initiatives to reduce inappropriate use of antibiotics should be implemented. The findings of this study may be generalisable to other LMICs in order to develop policies and guidelines to promote more appropriate dispensing and prescribing practices of antibiotics and limit the spread of antibiotic resistance.

Strength and limitation of this study

- This is the first study to investigate the pattern of antibiotic dispensing in private pharmacies in Nepal.
- Data on dispensing of medications including antibiotics was sourced directly from patients and validated from the dispensed medicines.
- Data were collected from a wide range of private pharmacies including high-end outlets staffed by pharmacists and small outlets staffed by drug retailers without formal health qualifications.
- Exit interviews were based on convenience sampling with interviews conducted between 9.00am and 5.00pm, thus may not be representative of all patients attending private pharmacies.
- Description of diagnoses or conditions by patients were symptom-based rather than disease-specific, which made it difficult to assess appropriate use of antibiotics and whether antibiotic dispensing and prescribing followed the standard guidelines.

Introduction

The role of the private sector in health care in low- and middle-income (LMICs) countries has often been neglected by governments and international public health communities (1). However, private pharmacies are widely established in most LMICs, and usually considered as a patient's first point of contact for healthcare and the preferred channel through which to get health services and medicines (2). These pharmacies range from high-end outlets to small, rural, road side stalls and can be staffed by fully trained pharmacists or a drug retailer or seller without formal health qualifications. Because of ease of access, more flexible opening hours, availability of cheaper medicines and credit (3) and personal intimacy (4), consumers often tend to utilise private rather than public facilities (5). Further, many patients have neither the time or money to consult a physician (6) preferring over-the-counter medicines and healthcare advice. About three in four antibiotic requests and three in five consultations in community pharmacies around the world result in the sale of antibiotics without a prescription (7).

Non-prescription use of antibiotics is associated with the risk of inappropriate drug use, defined as patients not receiving the appropriate medicines in doses that meet their individual requirements, for an adequate duration, and at the lowest cost (8). Inappropriate use of medicines is a serious global problem occurring in both developed and developing countries (9), with the World Health Organization (WHO) estimating more than half of all medicines are inappropriately prescribed, dispensed, or sold (8). This overuse and misuse of antibiotics is one of the main causes of antibiotics becoming ineffective (10), thus posing problems relating to treatment failure and other costs to the individual and society (11-13).

In Nepal, dispensing of medicines is undertaken by pharmacists and drug retailers or sellers and many dispensers have admitted treating patients too by also prescribing medicines (14). Pharmacists have three to five years of pharmacy education (14), however, drug retailers and sellers include individuals who are only associated with private pharmacies, do not necessarily have formal education in dispensing medicines, but can undertake training and obtain a licence to own and operate a pharmacy from the Department of Drug Administration (DDA), the government body dealing with medicines and their related affairs (15, 16). Practising healthcare without a license is illegal in Nepal (17), however many unlicensed pharmacies are also operating in remote areas of Nepal (18). Little is known about the antibiotic dispensing practices from licensed or unlicensed private pharmacies in Nepal. Previous studies conducted in Nepal that have examined antibiotic dispensing practices from private pharmacies have collected data directly from pharmacists or drug sellers themselves (18, 19), which may result in inaccurate reporting of dispensing practices. This study has investigated patterns of antibiotic dispensing through exit interviews with patients by reviewing their medication information, thus ensuring collection of reliable information. The findings of this study reveal issues about inappropriate use of antibiotics and can be used as a baseline against which to evaluate initiatives to improve antibiotic dispensing and prescribing practices in the private pharmacy sector in Nepal.

Methods

The study was a cross-sectional study conducted in the Rupandehi district of Nepal. This district was selected because it has an almost equal mix of urban and rural residents (20, 21) and a well-represented population of different castes and ethnicities with more than 63 castes/ethnicities residing in the district (22) out of 126 castes/ethnicities in the country (23). Within the district, there is varying access to transport, with good transport only available in urban areas, which is similar to other districts of Nepal.

Private pharmacies were selected based on WHO guidelines (24, 25). Before deciding on the private pharmacies, six survey areas were selected from the seven electoral areas in the district. 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. Altogether, six public health facilities were selected, two each from hospitals, primary healthcare centres and health posts, with the major hospital included as one of the hospitals (as per WHO guidelines). These health facilities were used as the basis for selecting the private pharmacies.

Private pharmacies to include in the study were selected from a list made available by the Nepal Chemists and Druggists Association (NCDA), Lumbini, Nepal. Separate pharmacies and pharmacies attached to private hospitals were included to represent both types. The NCDA list was verified after visiting each selected survey area and updated by deleting any duplicates in the list of pharmacies and adding any missing from the records. In total, 441 private pharmacies were in the NCDA list. Among them, 49 did not exist in the field while 31 were missing on the list. After adjusting the list for these pharmacies, 423 private pharmacies were included in the final list.

As outlined in the WHO guidelines, within each survey area, pharmacies on the final list were grouped according to whether they were located within or beyond five kilometres from each selected public health facility. Within each group in every survey area, pharmacies were assigned a number and then selected for inclusion in the study using a random number generator, with three private facilities selected from the within the five kilometres group and two selected from the greater than five kilometres group. Three private pharmacies were added to the original sample due to refusal of the initially selected pharmacies to allow data collection on the second day. Each pharmacy was surveyed for two days, other than the three that refused data to be collected on the second day and the three replacement pharmacies, which were surveyed for one day. Thus data collection covered 60 days with 33 private pharmacies (2 days per pharmacy for 27 pharmacies and 1 day per pharmacy for 6 pharmacies).

Data collection

Private pharmacies in Nepal do not follow the practice of keeping patients' records, so exit interviews were conducted with patients who had attended the selected pharmacies. Interviews were conducted from July 2017 to December 2017 from 9.00am to 5.00pm. The days allocated for data collection were based on the advice of pharmacists to obtain as representative a sample of days as possible. Patients were invited to participate based on convenience sampling, with as many patients as possible who attended the selected pharmacies approached to participate. In total 1,554 patients were approached, with 15 (1%) patients refusing to participate and 1537 patients included in the study. Individuals obtaining medicines on behalf of another person were excluded from the exit interviews as they may not have been able to provide the relevant details about the patient or their condition. In contrast, parents have these details for their children so children attending the pharmacies with their parents were included in the survey.

Data were collected using the Qualtrics Offline Surveys Application (26). Demographic characteristics of the patients for whom the medicines had been bought (age, sex), the disease or condition and sources of antibiotic (27) (self-medicated, recommended and supplied by a pharmacist or drug retailer without a prescription, prescribed by a doctor and dispensed by a pharmacist or drug retailer, other) were collected. Photographs were taken of the medicines, with no patient identifiers included, and attached to the Application. The maximum time taken for the exit interview was three minutes. Prior to the interview, all consumers were informed of the nature of the study and written consent was sought to interviews being conducted. Consent for patients younger than 18 years was sought from the accompanying parent or caretaker.

The principal researcher coordinated data collection and approached respective authorities and health facilities to obtain approval to collect the data, and four Nepali 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, the importance of ensuring 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 entered records in the Qualtrics Application.

Data analysis

The data were imported from the Qualtrics Application to MS-Excel spreadsheet for cleaning. The cleaned data were transferred to the SPSS statistical software (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: USA). Diseases or conditions collected from the interviews were generally described based on symptoms, thus similar symptoms were grouped together. For some analyses, the most commonly occurring groups (such as fever, respiratory symptoms and skin conditions) were separately analysed, with remaining groups combined into those likely to have an infectious cause ("other: infectious"), and those not

likely to have an infectious cause ("other: non-infectious"). Antibiotics were also grouped into classes for analysis (28). A core prescribing indicator, "*the percentage of patients prescribed an antibiotic*" was computed in line with the WHO's standard values (29). Descriptive analysis was conducted to show commonly dispensed antibiotics, sources of antibiotic, registration status of pharmacies and education of the pharmacist or drug retailer, and disease or condition. Chi square tests were performed to examine the association between antibiotic dispensing and explanatory variables including sex, age group of patient, sources of antibiotic and registration status of pharmacies and education status of the pharmacist or drug retailer. Logistic regression was also used to examine factors associated with antibiotic dispensing. An interaction term of sources of antibiotic with registration status and education was also examined. The significance level (α) was set at 0.05 for all statistical tests.

Patient and public involvement

No patients or public were involved in the design and conduct of the study.

Results

Characteristics of patients and prescription information

The sample comprised a similar number of male and female respondents, with all age groups relatively well represented (Table 1). Just over half of patients (55.2%) had a prescription from a doctor or health worker, with about one quarter not having a prescription but purchasing a medicine recommended and supplied by the pharmacist. Almost equal numbers of patients received their medicine from a pharmacist who had a diploma or bachelor's degree in pharmacy (49.6%) and drug retailers who had completed training from DDA (46.1%). The most commonly occurring diseases or conditions were fevers (18.1%), coughs (5.3%), and respiratory infection (4.9%). At least one antibiotic was dispensed in 947 (38.4%) patient encounters.

Table 1 Patient characteristics and information related to dispensing of medicines

Variables	Percentage	n_i/n_k [b,c]
Sex		
Male	50.5	776/1537
Female	49.5	761/1537
Age group of patient		
Less than 14 years	19.4	298/1537
15 to 24 years	20.2	310/1537
25 to 44 years	35.0	538/1537
45 and above years	25.4	391/1537
Sources of antibiotic		
Prescribed by a doctor or health worker and dispensed by a pharmacist or drug retailer	55.2	848/1537
Recommended and supplied by a pharmacist or drug retailer without a prescription	26.1	401/1537
Self-medicated	13.3	205/1537
Other (invalid prescription)	5.4	83/1537
Registration status/education		
Licensed/diploma or bachelors in pharmacy	49.6	762/1537
Licensed/training from DDA	46.1	709/1537
Unlicensed/education unknown	4.3	66/1537
Disease or condition*		
Fever	18.1	278/1537
Cough	5.3	82/1537
Respiratory infection	4.9	75/1537
Headache	4.8	74/1537
Loss of appetite	4.7	72/1537
Skin infection	4.6	70/1537
Common cold	4.4	68/1537
Injury	4.4	67/1537

	Acid peptic disease	4.3	66/1537
	Body ache	4.2	65/1537
	Heart disease	4.2	64/1537
	Fungal infection	3.8	59/1537
	Skin disease	3.7	57/1537
	Abdominal discomfort	3.6	55/1537
	Arthritis and bone pain	3.3	50/1537
	Others	21.8	335/1537
Prescribing indicator			
	Percentage of patients dispensed an antibiotic	38.4	590/1537
No of antibiotics dispensed			
	No antibiotic	61.6	947/1537
	One antibiotic	35.8	551/1537
	Two antibiotics	2.5	39/1537

[b] n_j *numerator*
[c] n_k *denominator*

DDA: Department of Drug Administration

Diseases or conditions included:
Fever: *Fever and pyrexia*
Cough: *Cough, dry cough and allergic cough*
Respiratory infections: *Acute respiratory infection, respiratory infection, chest infection and bronchitis*
Loss of appetite: *Weakness, anorexia and loss of appetite*
Skin infections: *Boils, dermatitis, wound and skin infection*
Common cold: *Common cold and sinusitis*
Injury: *Injuries*
Acid peptic disease: *Acid peptic diseases, gastritis, peptic ulcer, and upper gastrointestinal bleeding*
Body ache: *Body ache and backache*
Heart disease: *Heart disease and hypertension*
Fungal infection: *Fungal infection and ring worm*
Skin disease: *Skin diseases and skin allergy*
Abdominal discomfort: *Abdominal pain, nausea, vomiting and dyspepsia*
Arthritis and bone pain: *Arthritis, joint pain, leg Pain and shoulder Pain*

Commonly dispensed antibiotics

Among antibiotics, the most commonly dispensed were cefixime (16.9%), amoxicillin (12.2%), cefpodoxime (10.3%), ampicillin+cloxacillin (8.7%) and ciprofloxacin (8.7%). Cephalosporins (38.0%) were the most commonly dispensed class of antibiotics, followed by penicillins (29.3%), quinolones (13.7%) and marcolides (8.1%) (Table 2).

Table 2 Commonly dispensed antibiotics

	Dispensed antibiotics	No	%
1	Cefixime	106	16.9
2	Amoxicillin	77	12.2
3	Cefpodoxime	65	10.3
4	Ampicillin+Cloxacillin	55	8.7
5	Ciprofloxacin	55	8.7
6	Azithromycin	49	7.8
7	Metronidazole	48	7.6
8	Amoxicillin+Clavulanate	31	4.9
9	Cefadroxil	16	2.5
10	Cephalexin	16	2.5
11	Levofloxacin	14	2.2
12	Ofloxacin	14	2.2
13	Amoxicillin+Cloxacillin	11	1.7
14	Cefixime + Clavulanic Acid	11	1.7
15	Other	61	9.7
	Total	**629**	**99.6**

	Dispensed antibiotic classes	No	%
1	Cephalosporins	239	38.0
2	Penicillins	184	29.3
3	Quinolones	86	13.7
4	Marcolides	51	8.1
5	Antiprotozoal	50	7.9
6	Others	19	3.0
	Total	**629**	**100**

The percentage of antibiotics dispensed was highest for those patients for whom the medicine had been prescribed by a doctor or health worker (58%). It was also highest for patients who obtained their medicines

from an unlicensed pharmacy (59.1%). For several conditions, antibiotics were the most commonly dispensed medicine, including for respiratory infection (93.3%), diarrhoea and dysentery (91.3%), skin infection (87.1%), fever (70.5%) and urinary tract infection (57.9%).

The class of antibiotics dispensed was relatively similar by sources of antibiotic and registration status and education. Third generation Cephalosporins were the most common class of antibiotics recommended and supplied by a pharmacist or drug retailer without a prescription (40.7%) and prescribed by a doctor or health worker (38.1%), with Antiprotozoals the most common among patients who self-medicated (38.5%). Cephalosporins were also most commonly dispensed by both drug retailers who had training from DDA (41.3%) and those with a diploma or bachelors in pharmacy (36.1%). The highest dispensing rate of Cephalosporins was for the treatment of fever (69.5%), whereas penicillins were common for respiratory infection (60.8%), injuries (78.8%) and skin infection (67.2%) (Table 3).

Table 3 Descriptive analysis of dispensed classes of antibiotics by sources of antibiotic, registration status and education, and selected diseases and conditions

Variables	Antibiotics dispensed		Classes of antibiotics dispensed (%)					
	Yes = n (%)	No = n (%)	Cephalosporins = n (%)	Penicillins = n (%)	Quinolones = n (%)	Marcolides = n (%)	Antiprotozoal = n (%)	Others = n (%)
Sources of antibiotic								
Self-medicated	12 (4.2)	276 (95.8)	2 (15.4)	2 (15.4)	2 (15.4)	1 (7.7)	5 (38.5)	1 (7.7)
Recommended and supplied by a pharmacist or drug retailer without a prescription	86 (21.4)	315 (78.6)	35 (40.7)	14 (16.3)	12 (14.0)	8 (9.3)	14 (16.3)	3 (3.5)
Prescribed by a doctor or health worker and dispensed by a pharmacist or drug retailer	492 (58.0)	356 (42.0)	202 (38.1)	168 (31.7)	72 (13.6)	42 (7.9)	31 (5.8)	15 (2.8)
Registration status/education								
Licensed/diploma and bachelors in pharmacy	260 (34.1)	502 (65.9)	101 (36.1)	81 (28.9)	35 (12.5)	33 (11.8)	24 (8.6)	6 (2.1)
Licenced/training from DDA	291 (41.0)	418 (59.0)	128 (41.3)	90 (29.0)	39 (12.6)	16 (5.2)	26 (8.4)	11 (3.5)
Unlicensed/education unknown	39 (59.1)	27 (40.0)	10 (25.6)	13 (33.3)	12 (30.8)	2 (5.1)	0 (0.0)	2 (5.1)
Disease and condition*								
Respiratory infection	70 (93.3)	5 (6.7)	12 (16.2)	45 (60.8)	3 (4.1)	13 (17.6)	0 (0.0)	1 (1.4)
Diarrhoea and dysentery	42 (91.3)	4 (8.7)	4 (7.8)	0 (0.0)	10 (19.6)	0 (0.0)	37 (72.5)	0 (0.0)
Skin Infection	61 (87.1)	9 (12.9)	12 (19.7)	41 (67.2)	1 (1.6)	2 (3.3)	0 (0.0)	5 (8.2)
Fever	196 (70.5)	82 (29.5)	141 (69.5)	29 (14.3)	21 (10.3)	11 (5.4)	1 (0.5)	0 (0.0)
Urinary tract infection	22 (57.9)	16 (42.1)	1 (4.5)	0 (0.0)	18 (81.8)	0 (0.0)	0 (0.0)	3 (13.6)
Injury	33 (49.3)	34 (50.7)	4 (12.1)	26 (78.8)	2 (6.1)	1 (3.0)	0 (0.0)	0 (0.0)
Common cold	16 (23.5)	52 (76.5)	6 (37.5)	5 (31.3)	1 (6.3)	4 (25.0)	0 (0.0)	0 (0.0)
Abdominal discomfort	10 (18.2)	45 (81.8)	3 (27.3)	0 (0.0)	4 (36.4)	0 (0.0)	4 (36.4)	0 (0.0)
Skin disease	7 (12.3)	50 (87.7)	4 (57.1)	2 (28.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)
Cough	7 (8.5)	75 (91.5)	4 (40.0)	1 (10.0)	0 (0.0)	5 (50.0)	0 (0.0)	0 (0.0)
Other: infectious	104 (49.5)	106 (50.5)	38 (32.2)	29 (24.6)	23 (19.5)	14 (11.9)	6 (5.1)	8 (6.8)
Other: non-infectious	22 (4.5)	469 (95.5)	10 (43.5)	6 (26.1)	3 (13.0)	1 (4.3)	2 (8.7)	1 (4.3)

DDA: Department of Drug Administration

Diseases or conditions included:
Respiratory infection: *Acute respiratory infection, respiratory infection, chest infection and bronchitis*
Diarrhoea and dysentery: *Diarrhoea, dysentery and loose motion*

Skin infection: *Boils, dermatitis, wound and skin infection*
Fever: *Fever and pyrexia*
Injury: *Injuries*
Common cold: *Common cold and sinusitis*
Abdominal discomfort: *Abdominal pain, nausea, vomiting and dyspepsia*
Skin disease: *Skin diseases and skin allergy*
Cough: *Cough, dry cough and allergic cough*
Other: infectious: *Likely to have an infectious cause*
Other: non-infectious: *Not likely to have an infectious cause*

Factors associated with antibiotic dispensing

Across all diseases and conditions, antibiotic dispensing was significantly associated with age group, sources of antibiotic, and registration status and education of pharmacists (Table 4). Patients less than 15 years were more likely than all other age groups to receive antibiotics (p=<0.001). Those patients who attended a pharmacy without a prescription from a doctor or health worker were less likely to receive antibiotics than patients with a prescription (p=<0.001). In addition, patients were less likely to receive antibiotics from pharmacists who had a diploma or bachelors in pharmacy (p=0.001) compared to unlicensed drug retailers or licensed retailers with training from DDA only. The interaction term shows that patients who presented with no prescription were more likely to receive an antibiotic if they presented with no prescription to a pharmacy attended by a trained pharmacist.

Table 4 Factors associated with antibiotic dispensing

Variables	Antibiotics dispensing			Bivariable analysis			Multivariable analysis	
	Yes = n (%)	No = n (%)	X^2 (p-value)	n	OR (95% CI)	p-value	OR (95% CI)	p-value
Sex								
Male	302 (38.9)	474 (61.1)	0.187 (0.666)	776	1	0.666	1	0.576
Female	288 (37.8)	473 (62.2)		761	0.956 (0.778, 1.174)		0.934 (0.734, 1.188)	
Age group of patient								
Less than 15 years	177 (59.4)	121 (40.6)	98.876 (<0.001)	298	1		1	
15 to 24 years	116 (37.4)	194 (62.6)		310	0.409 (0.295, 0.566)	<0.001	0.464 (0.320, 0.672)	<0.001
25 to 44 years	210 (39.0)	328 (61.0)		538	0.438 (0.328, 0.584)	<0.001	0.432 (0.311, 0.602)	<0.001
45 and above years	87 (22.3)	304 (77.7)		391	0.196 (0.140, 0.273)	0.001	0.206 (0.142, 0.299)	<0.001
Sources of antibiotic								
Recommended and supplied by a pharmacist or drug retailer without a prescription (includes self-medication)	98 (14.2)	591 (85.8)	308.278 (<0.001)	689	0.120 (0.093, 0.155)	<0.001	0.087 (0.059, 0.128)	<0.001
Prescribed by a doctor or health worker and dispensed by a pharmacist or drug retailer	492 (58.0)	356 (42.0)		848	1		1	
Registration status and education								
Licensed/diploma and bachelors in pharmacy	260 (34.1)	502 (65.9)	11.627 (0.001)	762	0.698 (0.568, 0.859)	0.001	0.617 (0.465, 0.819)	0.001
Licensed/training from DDA (Includes unlicensed)	330 (42.6)	445 (57.4)		775	1		1	
Interaction term with sources of antibiotic, and registration status and education							1.987 (1.177, 3.354)	0.010

Discussion

In most developing countries, private pharmacies or drug stores are the first point of contact for people seeking healthcare (2). Antibiotics (and other prescription medicines) are readily available with or without prescription, and self-medication by patients is common. Non-prescription use of antibiotics is associated with a risk of inappropriate use due both to failure in dispensing in accordance with clinical guidelines and patients not using the drug appropriately (30). It is also one of the drivers of the emergence of antimicrobial resistance (31).

Findings of this study show the overuse of antibiotics dispensed from private pharmacies, with the percentage of patients dispensed an antibiotic (38%) being considerably higher than the level recommended by the WHO (20 to 26.8%) (29). This finding of overuse is consistent with studies conducted in private facilities in other LMICs including 43% in both India (32) and Uganda (33) and 53% in Bangladesh (34).

Unlicensed pharmacies, especially outside of cities, often exist in low- and middle-income countries (35). These pharmacies sell medicines informally and are not legally recognised by the health system of the countries in which they operate (36). While, practicing healthcare without a license is illegal in Nepal (17), weak regulatory oversight of the Nepalese health system encourages pharmacies to operate without licences. This study found the level of dispensing of antibiotics was higher by unlicensed drug retailers and drug retailers with limited training. Interestingly the interaction term in the multivariable model suggests that, while this is the case, if patients presented to a pharmacy with a trained pharmacist without a prescription, they were more likely to receive antibiotics. It has been suggested circumstances that drug retailers may approach dispensing of medicines as any other sales job, not wanting a customer to leave without making a purchase (35). More generally, inappropriate dispensing of antibiotics may occur due to the business motive of private pharmacies with profits from antibiotics contributing to total profit (37).

Third generation cephalosporins were the most common antibiotic type recommended and dispensed with or without prescription. The finding is consistent with the studies conducted in India showing cephalosporins were the most commonly supplied class of antibiotic in private pharmacies or clinics (32) and often used by urban private health facilities (38). Guidelines often 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 *Clostridium difficile, methicillin resistant Staphylococcus aureus (MRSA)* and other resistant infections (39, 40). Noticeably, third generation cephalosporins were dispensed to patients with minor symptoms, such as fever, which is self-limiting in most cases and could be a common symptom of several infections. The popularity of third generation cephalosporins lies in their lesser allergenic and toxicity risks as well as having a broad spectrum of activity (39). In Nepal treatment guidelines do not recommend cephalosporins as a first-line treatment for several infections such as respiratory tract infections, enteric fever, pneumonia and urinary tract infections (41).

Overprescribing and overuse of antibiotics in the treatment of respiratory infections and diarrhoea is a worldwide problem, potentially leading to widespread antimicrobial resistance (42). Contrary to international recommendations, this study found high prescribing rates of antibiotics for both conditions, suggesting possible overprescribing. The WHO guidelines recommend oral rehydration solution with other supplements for non-bloody diarrhoea (43) and home care without antibiotics for children with respiratory symptoms (44).

Across all conditions collectively, antibiotics were more likely to be dispensed to younger age groups especially less than 15 years of age compared to older groups. Respiratory diseases and diarrhoea impose a considerable health burden especially to children in LMICs (45, 46), and may lead to antibiotics being used more widely for the treatment of these diseases (47, 48). Higher self-medication practices among younger age groups could also be a factor contributing to higher antibiotic dispensing for younger age groups, with a study in Albania finding an association between self-medication and a higher use of antibiotics among younger age groups (49). Additionally increased education has been found to increase the risk of self-medication with antibiotics (50), and globally the literacy rates of young adults is higher than the elderly, with the differences is even wider in developing countries (51).

Policy implications

Levels of antibiotic prescribing above the WHO recommended rate suggests the need to implement measures to reduce potential inappropriate use in Nepal. Almost half of patients were dispensed antibiotics by drug retailers who, unlike pharmacists are professionally trained and do not have formal education in dispensing medicines. While this study did not examine their technical competencies, drug retailers should be encouraged to increase their skills through continued professional education.

In Nepal, prescribing is conducted by physicians and non-physicians such as auxiliary health workers and health assistants, who have 18 months to three years post-secondary training in diagnostics and therapeutics, and nurses (52). The physicians work at hospitals and non-physicians, who are referred to as health workers, mostly work in public health facilities at the community level and have their own private pharmacies. Health workers are less qualified than physicians but are authorised to prescribe medicines as outlined in the antibiotic treatment guidelines (41). However, such guidelines are barely in practice or monitored (53). WHO's guideline of good pharmacy practices confines the role of pharmacists to dispensing only (54). A general lack of enforcement of the legislation covering registration of pharmacies and the distribution of antibiotics facilitates the inappropriate use of antibiotics in Nepal. Stronger enforcement mechanisms of pharmacy registration and restricting pharmacists and drug retailers supplying antibiotics without prescription should be established.

Private pharmacies are widely established in most LMICs including Nepal. They are usually considered as a patient's first point of contact and preferred channel to receive health services (2) particularly given issues relating to the unavailability and inaccessibility of quality of care from public health facilities (55). Private pharmacists and community members are often known to each other and pharmacists can be under pressure to supply antibiotics (56). Pharmacists and drug retailers generally do not charge consultation fees and profits from selling drugs is a main source of their income (57), which could encourage the selling of antibiotics since it is one of the more profitable medicines (37). A targeted intervention to provide education and training relating to antimicrobial resistance and supplying antibiotics only with prescriptions will lead to greater consideration of antibiotic dispensing practices based on the standards of good pharmacy practices, thus contributing to a reduction in the risk of development of antibiotic resistance bacteria.

Additionally, the relatively high prescribing rate of third generation cephalosporins in private health facilities in Nepal is of concern, given that these classes 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 (58) to prevent drug-resistant bacteria developing. Educational interventions to reduce inappropriate dispensing or prescribing of antibiotics in unwarranted situations should include guidance on the proper selection of antibiotics.

Strengths and limitations

Limited evidence is available in regard to the pattern of antibiotic dispensing in LMICs. This study has provided an evidence base about the current pattern of antibiotic dispensing from private pharmacies in Nepal, with data on dispensing of medications including antibiotics sourced directly from patients and validated from the dispensed medicines. Data on dispensed medicines were collected from a wide range of private pharmacies including high-end outlets staffed by pharmacists and small outlets staffed by someone without formal health qualifications. The information on dispensed medicines provides a useful baseline against which to measure the effectiveness of future policies and programmes to reduce the level of inappropriate dispensing of antibiotics. The findings of the study also reinforces calls to build a strong regulatory environment in advancing prudent antibiotic use. The findings may also be applicable to other low and middle income countries, where the health system is similar to Nepal.

However, the study has several limitations. The study covered about 8% (33/423) of private pharmacies in the Rupandehi district. While the selection process followed WHO guidelines, these guidelines do not account for the number of facilities in the district, thus the sample of pharmacies selected may not be representative. Interviews were conducted between 9.00am and 5.00pm at the selected pharmacies, which excludes patients attending the pharmacies at other times, and exit interviews were based on convenience sampling. Diagnoses or conditions of patients were non-specific and recorded based on the understanding of the patients. Description of diagnoses or conditions were more symptom-based and 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 dispensing and prescribing followed the standard guidelines. Another limitation is that the Rupandehi district lies in a low-land region of Nepal, which has a greater availability of health services than in hill and high-hill regions. Results of the study are thus more generalisable to districts falling in low-land regions than hill and high-hill regions, a factor which needs to be considered in using findings from the study in developing and implementing policy to improve pharmacy practice in Nepal and similar countries.

Conclusion

This study documents antibiotic dispensing practices in private pharmacies in Nepal that were high compared with WHO guidelines. The overuse of antibiotics has been associated with a higher prevalence of antimicrobial resistance. Given global concerns about antimicrobial resistance, evidence relating to overuse and misuse in Nepal provides a rationale to consider introducing initiatives to reduce inappropriate use of antibiotics. Additionally this evidence may be more widely generalisable to other countries with similar health system financing arrangements.

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STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Title: *Survey of the pattern of antibiotic dispensing in private pharmacies in Nepal*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any pre-specified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3 and 4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3 and 4
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	3 and 4
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	3 and 4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	3 and 4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	3 and 4
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	4
		(*b*) Describe any methods used to examine subgroups and interactions	4

		(*c*) Explain how missing data were addressed	4
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	3 and 4
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5 and 6
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	5 to 9
		(*b*) Report category boundaries when continuous variables were categorized	5 to 9
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10 and 11
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.