Quality of Drugs and Drug Use Patterns at Different Level of Health Care Settings in Nepal, 2016

Government of Nepal

Nepal Health Research Council

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October, 2017

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Ramshah Path, Kathmandu, Nepal

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Authors

Khem Bahadur Karki, Krishna Kumar Aryal, Pradip Gyawali, Arpana Pandit, Raj Kumar Thapa, Jasmine Maskey, Ranju Mehta, Purna Chandra Poudel, Mona Giri, Trishna Acharya, Neelam Dhakal, Baburam Humagain

Recommended citation

Karki KB, Aryal KK, Gyawali P, Pandit A, Thapa RK, Maskey J, Mehta R, Poudel PC, Giri M, Acharya T, Dhakal N, Humagain B. Quality of Drugs and Drug Use Patterns at Different Level of Health Care Settings in Nepal, 2016. Kathmandu, Nepal. Nepal Health Research Council, 2017.

ACRONYMS

AHW	Auxiliary Health Worker
AMR	Anti-microbial Resistance
ANM	Auxiliary Nurse Midwife
BCG	Bacille Calmette Guerin
BP	British Pharmacopeia
BSC-IV	Biopharmaceuticals Classification System IV
CMA	Community Medical Assistant
DH	District Hospital
DPT	Diphtheria, Pertusis, Tetanus
EDL	Essential Drug List
GoN	Government of Nepal
HP	Health Post
IP	Indian Pharmacopoeia
MoH	Ministry of Health
MoHP	Ministry of Health and Population
NDP	National Drug Policy
NHRC	Nepal Health Research Council
PHC	Primary Health Care
PHCC	Primary Health Care Center
PHCRD	Primary Health Care Revitalization Division
SHP	Sub-Health Post
SPSS	Statistical Packages for Social Sciences
SSFFC	Substandard, Spurious, Falsely labeled, Falsified and Counterfeit
USP	United States Pharmacopoeia
WHO	World Health Organization

ACKNOWLEDGEMENT

I am grateful to all the members of the study team for their individual contribution at different aspects of the study in the process of completing it and producing this report.

I would like to offer my sincere thanks to Dr. Khem Bahadur Karki, Mr. Baburam Humagain, Dr. Krishna Kumar Aryal, Dr. Pradip Gyawali , Ms. Arpana Pandit, Ms. Trishna Acharya and Ms. Neelam Dhakal co- investigators of the study for conceptualizing, designing and implementing this study.

My special thanks go to the field supervisors and enumerators of this study for their tireless work during data collection and drug sample collection. I am also thankful to all those who participated in the survey and to the community leaders, Female Community Health Volunteers, Chief of the District Public Health Office and health facilities' in-charge of the selected districts for their support in implementing the study.

I must thank to the staffs of District Hospitals, Health Posts and Primary Health Centers for their support and cooperation during the study. Furthermore, I would also like to thank all the staffs involved in data entry. I am thankful to our Research Officers Mr. Bihungum Bista , Mr. Purna Chandra Poudel , Ms. Mona Giri , Ms. Jashmine Maskey and Mrs. Ranju Mehta who supported to study team in different phases of research project. I would like to acknowledge the laboratories for carrying out the tests of the medicines provided to them for testing the quality in terms of specified characteristics. They also owe great thanks for maintaining the privacy and confidentiality in the analysis of samples.

I also thank Mr. Subodh Kumar Karna, Deputy Chief Account Controller, Mr. Nirbhay Kumar Sharma, Deputy Chief Admin Officer, Mr. Bijay Kumar Jha, Training Officer , Mrs. Namita Ghimire, Research Officer, Ethical Review, Monitoring and Evaluation Section and the entire staffs of Nepal Health Research Council for their support to undertake the project and complete it successfully.

Prof. Dr. Anjani Kumar Jha

Executive Chairman

Nepal Health Research Council

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EXECUTIVE SUMMARY

Background: Drug quality has direct impact on patient's health. The drug should be of standard quality in order to meet its therapeutic efficacy. The poor quality of drug results negligible to detrimental effect on human's health. Burgeoning various health issues and dampening medicine efficacy has questioned whether the drug being administered is appropriate and of standard quality in every individuals. In addition to quality of drug, rising cases of irrational use of the drugs and lack of patient compliance are other key factors which directly contribute in diminishing drug efficacy. This study aims to assess the quality of drug and drug use pattern at different level of health settings in Nepal.

Method: It was a descriptive cross sectional study. Out of the total listed health facilities from 5 developmental regions, 90 health facilities (1 District Hospital, 1 Primary Health Care Centre, 4 Health Posts from each district) representing three geographical areas from each developmental region was chosen randomly. Thirty patients from each selected Health Post and Primary Health Care Centre and 50 patients from each District Hospital were identified prospectively. To assess prescribing and dispensing practice of the drug, exit client interview was taken with individual patient from each selected health facility.

In order to analyze the quality of drug, 10 generic medicines, each of 5 different brands were collected randomly from three private licensed pharmacies nearest to each selected government facilities. Also, free essential drugs supplied by the Government of Nepal was collected on the scientific basis i.e. Biopharmaceuticals Classification System IV (BCS-IV) drugs, frequency of prescription, therapeutic category from selected districts. Similarly, face to face interview was also taken with health facility in-charge of selected health facility using structured questionnaire and required data were collected to determine the storage condition of the drug.

Data were entered and managed in Epidata, further cleaned on Microsoft excel 2007 and analyzed using the SPSS version 20. Descriptive analysis was presented on number and percentage in tabular form. Written informed consent was taken from each patient and for children less than 14 years consents were taken from their parents.

Results: Among total prescribed drugs from all health facilities, 60.71 % of drugs were found to have been prescribed with generic names and highest percentage were reported from District Hospitals. Next, among total prescribed drugs 68.91% were found to be essential drug while 23.74 % of drugs were found to be antibiotics. Out of total drugs that were dispensed from each health facilities, only 51.81 % of drugs were found to have been dispensed in sufficient quantity. And among those patients, who were dispensed medicines only 49% were found to have complete knowledge about medicine and its use. Further, there was no implementation of standard measures for storage of drugs in health facilities. Also, 26 % of health posts were found not storing vaccines in cold chain.

Among total drugs sent for in-vitro analysis in two laboratories, Paracetamol 500 mg BP (Cetophen) supplied as essential drug by Government of Nepal was found substandard. Further, other eight drugs including two essential drugs supplied by Government of Nepal (GoN) and six non-essential drugs supplied from private sectors failed to meet required standard in one laboratory. Similarly, large variations in price were reported among different brands of same generic medicines. There were almost 400 % variations in price among different brands of Tamsulosin 0.4 mg capsule, Cefixime 200 mg Tablets and Amlodipine 5mg Tablets.

Conclusions: Drugs are prescribed with generic names from majority of health facilities especially by District Hospitals. Only half of the patients are dispensed complete prescribed medicines and among those who are dispensed medicines, majority lack complete knowledge regarding medicine use. Similarly, some of the drugs are found to be substandard in Nepalese market. The widely used drug Paracetamol 500 mg BP (Cetophen) supplied as essential medicine by GoN is found substandard. In addition to this, other eight drugs including two essential drugs supplied by GoN and six non-essential drugs supplied by private sectors are also found substandard. Similarly, there are large variations in price among drugs of different brands of same generic. Few variations can also be seen in terms of expiry date. Health facilities have not fulfilled all the criteria of standard storage system of drugs. In addition, few health posts do not even store vaccines in cold chain.

Chapter 1

Introduction

1.1 Background

Nepal National Drug Policy 1995 defines "drug as any substance which is intended to be used in human beings or animals for diagnosis, treatment, cure, mitigation and prevention of diseases or for promotion of health or for the destruction of microorganisms which have caused disease or to affect the physical structure or function of a body" (1). The drug should be of standard quality in order to meet its therapeutic efficacy. The poor-quality of drug which includes substandard, spurious, falsely labeled, falsified and counterfeit (SSFFC) can have minor to detrimental effect on humans health (2). The problem of SSFFC medicines is found to be more persistent on developing countries. Their prevalence increasingly threatens public health by jeopardizing patient safety, leading to treatment failure, contributing to development of drug resistance, and possibly leading to diminished confidence in health systems (3). Similarly, transportation, handling and storage of drugs also have direct impact on the quality of drug. Drugs should be stored properly at adequate temperature and humidity protecting from sunlight.

Drug utilization research has been defined by the WHO as "the marketing, distribution, prescription and use of drug in a society, with special emphasis on the evidence of irrational drug use (4). In case of developing countries rather more intensive irrational practices of drugs are seen in health sector. In Nepal, the essential health services are provided by the government through Primary Health Care Center (PHCC). Facilities are separated into three levels i.e. Primary Health Care, secondary health care system and tertiary health care system. It delivers services up to the grass root level in rural and urban areas of the country.

Access to medicines is the fundamental right to every citizen of Nepal. The Alma-Ata declaration during the International Conference on Primary Health Care in 1978 provided a guiding framework for public health initiatives (5). Its declaration included appropriate treatment of common diseases and injury, and the provision of essential drugs are two vital components of primary health care concept. The provision of drugs is the component that the patient most demand and expect.

Since 2007, Nepal has adopted a policy of free health care services to the poor and vulnerable citizens attending primary health care centers and district hospitals (up to25–bedcapacity) as a targeted exemption provision from 2007; additional free outpatient services were also offered to the same groups from the district hospitals in 35 districts on the basis of lowest ranked Human Development Index from 2008. Then after six months, universal free health care provision was implemented at Sub-Health Post and Health Post level. Now all the sub-health Posts have been upgraded to Health Posts. A second universal program commenced in January 2008 aimed the provision of free essential health care services to all citizens (6). Government of Nepal in the Interim Constitution of 2007 as well as in the recently promulgated Constitution of Nepal 2015 addressed health as a fundamental right (7).

Primary Health Care Revitalization Division (PHCRD) of Department of Health Services has made some provision of fund for the treatment of all patient related to target groups at central, regional, sub-regional and zonal hospital. PHCRD has also made an amendment in the policy by adding the number of distributed medicine from 32 to 36 at HP, 35 to 58 at PHC and 40 to 70 items at hospital level (8) which is implemented now in all districts over Nepal.

Cases of treatment failure and development of resistance are burgeoning worldwide (9).The major contributing factors are: drug failing to meet standard quality, irrational use of drugs, anti- microbial resistance (AMR), non-compliance to medicine, lack of patient's knowledge to information of medicines, unavailability of sufficient medicines and so on. Irrational use of drug is a major problem that is growing throughout the world. The rational use of drug requires that patients receive medicine appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time and at the lowest cost to them and the community (10). It includes correct diagnosis, appropriate indication, prescribing the right drug to the right patient, providing appropriate information, dispensing and monitoring. The aftermath of various evidences like- poly-pharmacy, overuse, underuse and misuse of medicines, inappropriate antimicrobials use etc. ultimately leads to irrational drug use.

Similarly, AMR is another burning problem that is emerging globally. The major causes for AMR are: overuse, inappropriate prescribing, non-compliance, extensive use in agriculture, failure to develop new antibiotics etc. To draw attention towards major issues, Ministry of Health and Population (MoHP), WHO and other partners in Nepal, had celebrated World Antibiotic Awareness Week between 16 and 22 November 2017 (11). Antibiotics fall under group "kha" of drug category and should be dispensed only under prescription. But, in developing countries like Nepal, especially in remote areas, where accessibility to health care centers and medicines is not practicable, people are compelled to take any antibiotics that are available to them. Thus, this irrational practice of antibiotics culminates into resistance to antibiotics.

In addition to this, improper prescription filling and dispensing of medicine also affect the quality of

health care. Next, prescribing cascade is also another contributing factor for affecting quality of health care which is the result of misinterpretation of adverse drug reaction as a new medical condition and prescribing new medicines to treat that condition (12).

Every patient has right to get information of the medicine. To ensure the right of every individual to essential medicines, WHO launched the concept of essential drug list in 1977 which is being periodically revised and updated till date. The WHO defines essential drugs as "those that satisfy the health care needs of the majority of the population; they should therefore be available at all times in adequate amounts and in the appropriate dosage forms (13). To promote the quality in health care, Nepal also published its first essential drug list in 1986 A.D. Essential Drug List aims to satisfy the priority health care needs of the population and to ensure a higher quality of care, better management of medicines (including improved quality of prescribed medicines), and a more cost-effective use of available health resources. The National Drug Policy 1995 has also listed in its strategy to use the essential drug list at all levels of health facilities including central and referral hospitals and manage the procurement, storage and distribution system accordingly. It also aims at producing 80% of the essential drug formulation within 10 years in the country (14). Essential Drug List of Nepal 2016 includes 70 medicines for District Hospital, 60 medicines for primary health care centers and 34 medicines for Health posts (6).

1.2 Rationale of the study

The irrational use of drugs has become the worldwide problem than the absence of drug information. These practices are mostly common and costly in developing countries. Such Practices include poly pharmacy (more than one medicine is used unnecessarily), use of wrong or injective medicines, or underuse or incorrect use of effective medicines. Similarly, reports on treatment failure and drug resistance are frequent because of substandard/counterfeit drugs. The other possible reasons are drug's chemical instability, inappropriate storage and transport, and poor quality control during manufacturing. The quality of some pharmaceutical products that are exported to the least developed countries sometimes fail to comply basic quality standards (15). In Nepal, large proportions of the population have limited accessibility to medicines (i.e geographical, financial) as well as poor availability of medicines at health facilities. The availability of drugs in the Grass root level including Health Post and clinics are sporadic resulting in the prevalence of inappropriate drug use. The other issues that complicate the rational use of drugs are illiteracy and the geo-graphical barriers, remote and rural populations are not able to access the health facilities (16).

Generally, the irrational use of drugs are numerous and complex involving the health system, prescriber, dispenser, patient and the community. Prescribing error leads to ineffective and unsafe treatment, exacerbation or prolongation of illness, distress and high costs. Along with these, counterfeit drugs or poor quality of drugs may lead to several implications to public health (2).

In Nepal limited studies have assessed the pattern of drug use practices in different level of health care

settings. However, it is important to assess the drug use situation and the quality of drugs in health facilities that provides more complex health services. The current study is aimed at assessing the quality of drugs, along with prescribing and dispensing practices of Nepal.

1.3 Objective of the study

1.3.1 General Objective

The general objective of this study was to assess the quality of drugs and drug prescribing pattern at different level of health settings in Nepal

1.3.2 Specific objectives

- To identify the storage condition of drugs in health facilities.
- To assess the quality of drugs available at public and private health facilities.
- To assess prescribing practice of drugs in different health facilities.
- To assess dispensing practices of drugs in health facilities.
- To find out drug compliance knowledge among patients in different health facilities.

Chapter 2

Methodology

2.1 Study Design

This study was designed as a descriptive cross sectional study to assess the quality of drugs and drug use practice in different level of health care settings in Nepal.

2.2 Study Site

This study was carried out in 15 districts representing eco-development regions. Rationale for the selection of districts was based on NDHS survey 2011. Selected districts were listed below :

Eastern Development Region	Central Development Region	Western Development Region	Mid-Western Development Region	Far-Western Development Region
Panchthar	Dhading	Argahakanchi	Dailekh	Baitadi
Solukhumbu	Dolkha	Mustang	Mugu	Bajhang
Siraha	Parsa	Nawalparasi	Bardiya	Kanchanpur

2.3 Study Population

The surveyed population included patient from each selected health facility who had been living at their place of residence for at least six month. People with the following characteristics were not included:

- Participants not providing informed consent for the study.
- Mentally ill and not able to provide informed consent.
- Those with hearing and visual disabilities.

Health facility in-charges from selected health facilities were also included under study population.

2.4 Sample Design

The sample size was calculated to represent the entire target population and health facility in Nepal. In order to achieve this statistical inference, the sample size was calculated using the reference of "WHO operational package for assessing, monitoring, and evaluating country pharmaceutical situation-2007" (17)**.** Out of the total listed health facilities, 90 health facilities (1 district hospital, 1 Primary Health Care Centre, 4 health post from each cluster) representing three geographical areas were chosen randomly from selected districts. For the selection of patients, 30 patients from each selected Health Post and Primary Health Care Centre and 50 patients for each district hospital was identified prospectively.

2.5 Sampling Technique:

Multistage sampling technique was used to identify the districts from development region. From each domain, districts were divided into three strata according to ecological belt. Random sampling technique was used to identify the districts. Fifteen districts were identified representing the eco-development region. Probability proportionate to size was applied to select the health facilities and to improve the survey estimates. Both public and private pharmacy were covered to identify the national scenario. Sampling of private pharmacies entailed selecting three private licensed pharmacies nearest to each selected government facility randomly. Prospectively, patients from each health facility interviewed at the exit while drugs are dispensed.

From the selected districts, free essential drugs which are supplied by government of Nepal was collected on the scientific basis i.e. (BCS-IV) drugs, frequency of prescription, therapeutic category and quality analysis examination of the selected drugs was done. Checking and verification of drugs availability and expiry date was done for all free essential medicines, for that particular facility.

2.6 Data Collection Procedure:

2.6.1 Training of Data Collection Team

Four days training was organized in Nepal Health Research Council, prior to the training, the enumerators were properly oriented on the meaning of the tool and how to probe the questions, to ensure accurate response. The training focused on interview techniques, sampling process, and the drugs sample collection process.

2.6.2 Data Collection Technique:

Individual face-to face interview was conducted with the patient, the prescriber and dispenser. A standard questionnaire was used following the WHO guidelines and protocol. Post Market Surveillance was done to collect the drug sample from the selected health facilities.

For the collection of prescription, either photocopies of the prescription or the image was taken for further analysis. Trained and oriented enumerators were hired for data collection. Data collection was

carried out using the questionnaire or the checklist according to the WHO guidelines and protocol.

For collection of drug samples, 3 three private licensed pharmacies nearest to each selected government facility were randomly selected and following 10 different molecules each containing 5 different brands were collected.

Table 1: List of collected drugs

SN	Generic name	Dosage form	Quantity	Number of Brands
1	Esomeprazole 40 mg	Capsule	130	5
2	Ciprofloxacin 500 mg	Tablet	130	5
3	Ofloxacin 400 mg	Tablet	130	5
4	Cloxacillin 500 mg	Tablet	130	5
5	Metformin 1000 mg	SR tablet	130	5
6	Losartan 50 mg	Tablet	130	5
7	Cefixime 200 mg	Tablet	130	5
8	Azithromycin 500 mg	Tablet	130	5
9	Tamsulosin 0.4 mg	Tablet	150	5
10	Amlodipine 5 mg	Tablet	150	5

2.6.3 Field Management

The field manpower for data collection comprised 45 individuals divided into 5 groups. Each team consisted of one field supervisor and 8 enumerators. Enumerators had an academic background either in nursing, pharmacy and public health. Their major responsibility was to fill out the questionnaires and to collect the drug sample. A field supervisor was appointed as a team leader for overall field management and to coordinate with respective authorities at the field level, ensure completion. Furthermore, field supervisors also carried out on the spot checks of the information collected by enumerators to ensure the quality of data.

2.6.4 Quality Control

This study adopted the tools based on WHO guidelines and protocol. The English version of the instrument was translated back into Nepali and survey results translated back into English. Before, finalization of tools pre-testing was done in the Health Post and Primary Health Care Centre of Kathmandu Valley with 20 participants. At the end of data collection, participant's feedback was obtained and all the comments compiled into a single report and used to refine the instrument. Then revised instrument in Nepali was endorsed by the expert prior to use in the field.

2.7 Data Processing and Analysis

Regular checking for consistency and completeness was undertaken. The field supervisors checked the completed questionnaire of the day during evening and provide feedback in each day. Database

was prepared in Epidata for data entry. Consistency and quality of data was maintained. Data cleaning and editing was done subsequently after entry and analysis was done using SPSS version 20.0.

2.8 Ethical Consideration

This study was approved by the Ethical Review Board of the Nepal Health Research Council. Formal Permission was taken from the concerned authorities in the selected districts. An informed written consent was obtained from all the participants and health facilities in-charge. The objectives of the research were explained in simple language and participants were also provided with an information sheet containing the research objectives, data collection method, role of participants and personal and community benefits as well as any possible harm to the participants. The confidentiality of the information gathered was maintained.

Chapter 3

Findings

3.1 Results related to prescribing and dispensing

Table 2 : Characteristics of prescribed drugs in different health facilities

Characteristics	Health facility							
	DH(n=15)		PHC(n=15)		HP(n=58)		Total(N=88)	
	n	%	n	%	n	%	N	%
Drug prescribed with generic name	2280	47.98	1097	57.52	2798	72.34	6175	60.71
Essential drug prescribed	2280	56.45	1097	66.55	2798	79.98	6175	68.91
Antibiotics prescribed	2280	20.175	1097	23.79	2798	26.63	6175	23.74
Drug dispensed in sufficient quantity	1168	51.97	633	54.82	2002	50.89	3806	51.81
Patients' knowledge on medication	1168	49.74	633	45.49	2002	49.95	3806	49.18

The above table illustrates the percentage distribution of prescribed drugs in different health facilities. Among total prescribed drugs from all health facilities, 60.71 % of drugs were found to have been prescribed with generic names. On comparing three health facilities, health posts constituted greatest percentage of drugs that were prescribed with generic names. Similarly, out of total prescribed drugs, 23.74 % of drugs were antibiotics and 68.91% were identified as essential drugs. Next, among total dispensed drugs from each health facilities, only 51.81 % of drugs were found to have been dispensed in sufficient quantity. Moreover, only 49% of patients who were dispensed medicines from different health facilities were found to have proper knowledge about medicine and its administrations.

Table 3: Distribution of personal primarily engaged in examining patients at different health facilities

Responsible person for examination	Health Facility			
	DH(n=15) %	PHC(n=15) %	HP(n=58) %	Total (N=88) %
Doctor	100	60	-	27.3
Health Assistant	-	40	36.2	30.7
CMA	-	-	44.8	29.5
AHW	-	13.3	25.9	19.3
Staff nurse	-	6.7	1.7	2.3
ANM	-	13.3	6.9	6.8

The above table depicts the percentage distribution of personnel primarily involved in examining patients at different health facilities. Doctors were identified as primary examiner in all district hospitals. Besides doctors, health assistants were also found as primary examiner in 40 % of PHC. Furthermore, CMAs were found to have been engaged primarily in most of the health posts (45%) followed by health assistants and AHW in some health posts (36% and 26% respectively).There were no involvement of any doctors in HP.

Table 4: Distribution of Personnel involved in dispensing

Responsible for dispensing	Health Facility			
	DH(n=15) %	PHC(n=15) %	HP(n=58) %	Total(N=88) %
Doctor	-	-	-	-
HA	20	13.3	15.5	15.9
CMA/AHW	46.7	53.3	70.7	63.6
Staff nurse/ANM	26.7	60	44.8	44.3
Assistant pharmacist	13.3	-	-	2.3
Pharmacist	13.3	-	-	2.3
Others	-	6.7	-	1.1

The above table depicts the percentage of health facilities encompassing different personnel for dispensing medicines. Among all the personnel, CMAs/AHWs were found as a major personnel involved in dispensing in all the health facilities (District Hospital, PHC and HP) followed by staff nurse/ANM who were identified to have been involved in 27 % of District Hospital, 60 % of PHC and 45% of HP.

3.2 Results related to drug quality

3.2.1 Assessment of drug storage

Table 5: Availability of vaccine at different health facilities

Available vaccine	Health Facility			
	DH(n=15) %	PHC(n=15) %	HP(n=58) %	Total(N=88) %
BCG	73.3	73.3	72.4	72.7
DPT	73.3	73.3	74.1	73.9
MR	73.3	73.3	74.1	73.9
TT	80 .0	80.0	74.1	76.1
Polio/PV	73.3	73.3	74.1	73.9
JE	66.7	40.0	44.8	47.7

The above table shows the percentage of availability of vaccines among different Health Facilities. It was found that Bacille Calmette Guerin (BCG),Diphtheria Pertusis Tetanus (DPT), Measles Rubella (MR) and Polio vaccines were available in approximately 74 % of all health facilities. However, Tetanus Toxoid (TT) vaccine was found to have been available in slightly greater number of facilities: 80 % of DH and PHC. Similarly, Japanese Encephalitis (JE) vaccine was available in least number of health facilities comprising 67 % of DH, 40 % of PHC and 45 % of HP.

Table 6: Places used for storing vaccines in different health facilities

Place of vaccine stored	Health Facility			
	DH(n=15) %	PHC(n=15) %	HP(n=58) %	Total(N=88) %
Refrigerator	100	60	17.2	38.6
Cold Chain	-	33.3	12.1	13.6
Other	-	-	24.1	15.9

The above table demonstrates the percentage of different health facilities which used different locations for vaccine storage. In total, 39 % of health facilities were identified to have used refrigerator for storing vaccines among which in all district hospitals, vaccines were found to have been stored in refrigerators only, while only 60 % of PHC and few HPs (17%) were identified having refrigerator for storing vaccines. Next, cold chain was found to have been practiced by 33 % of PHC and 12% of HP. Besides, few health posts were also found practicing other methods for storing vaccines.

Table 7: Methods for storing drugs in different health facilities

Methods of drug storage	Health Facility			
	DH(n=15) %	PHC(15) %	HP(58) %	Total(88) %
Sunlight protected	33.3	13.3	34.5	30.7
Moisture protected	66.7	86.7	79.3	78.4
Heat protected	100	93.3	93.1	94.3
Well ventilated	60	73.3	75.9	72.7
Sanitation	53.3	80.0	79.3	75

The above table indicates the percentages of health facilities which used different methods for storing drugs. Majority of health facilities (94%) were identified to have followed heat protection method for storing drugs and among which all the district hospitals were found to have followed this method. Similarly, some health facilities (78%) were also found to have used moisture protection method for storing drugs. In addition to this, few health facilities (31%) were also identified using sunlight protection method for drug storage.

Table 8: Technique used for managing expired drugs at health facilities

	Health Facility			
	DH(n=15)	PHC(n=15)	HP(n=58)	Total(N=88)
Practice for expired drug	%	%	%	%
Separating medicine	40	26.7	24.1	27.3
Burning	53.3	60	63.8	61.4
Burring	33.3	33.3	44.8	40.9
Return to suppliers	6.7	-	3.4	3.4

The above table depicts the percentage of health facilities which used particular techniques to manage expired drugs. More than 60 % of health facilities were identified practicing burning of drugs for management of the expired drugs followed by burring of expired drugs by 41% of health facilities. Least (3%) were also found to have been involved in returning expired drugs to the supplier.

3.2.2 In-vitro analysis

Table 9: Total sample sent to lab

Laboratory code	Number of samples
Lab I	87
Lab II	127
Total	**214**

In total 214 samples of drug (different brands of 45 generic drugs) were sent to laboratories for in-vitro analysis of the sample and among them 42 samples were common to both labs. Out of total samples, 91 samples were domestic and 123 were imported.

Table 10: Categorization of sample sent to lab

Categories	Lab I	Lab II	Total
Government of Nepal (GoN)	10	16	26
Private sectors	77	111	188
Total	87	127	214

Out of total samples, 26 samples were supplied from Government of Nepal and 188 samples were from private sectors.

Table 11: Regulatory compliance on labeling

Regulatory Parameters (n=214)	Percentage (%)
Manufacture date mentioned	100.0
Expiry date mentioned	100.0
Batch number mentioned	100.0
Direction for use	19.2
Caution mentioned	79.4
Storage condition	95.8

The above table shows that most of the products complied with the existing regulatory requirement on labeling which is mentioned in schedule 5 of Drug Standard Regulation, 2043 (18).

Table 12: Regulatory classification of drugs studied

Classification (Schedule)	Percentage (%)
Samuha Ga	10.3
Samuha Kha	47.2
Samuha Not mentioned	19.6
Schedule H	20.6
Schedule H1	2.3

Table 13: Consumer price of selected generics

Generic	No of brands	PriceMax	Price Min	Average of min & max	Max variation %
Amlodipine 5mg Tablets	16	14.08	2.90	8.49	385.5
Azithromycin 500 mg Tablets	17	45.00	25.00	35.00	80.0
Metormin HCl ER	3	6.00	5.85	5.93	2.6
Metformin HCl	3	4.98	1.80	3.39	176.7
Ofloxacin 200mg	2	8.00	4.86	6.43	64.6
Cefixime 200 mg Tablets	10	30.00	6.00	18.00	400.0
Cefixime 200mg dispersible	3	28.00	11.25	19.63	148.9
Ciprofloxacin 500 mg Tablets	19	12.29	4.20	8.25	192.6
Esomeprazole 40 mg Tablets	8	12.00	10.00	11.00	20.0
Losartan Tablets 50 mg Tablets	12	13.50	4.98	9.24	171.1
Ofloxacin 400mg	10	16.00	11.57	13.79	38.3
Tamsulosin 0.4 mg capsule	3	60.00	12.00	36.00	400.0

The above table illustrates the variation in price among different brands of same generics. The maximum variations in price were identified in Cefixime tablets and Tamsulosin capsule (almost 400 %) followed by Amlodipine tablets.

Table 14: Difference in self-life claim

Drugs	Self-life
Albendazole	3-4 years
Amlodipine Tablets	2-3 years
Atenolol Tablets	2-3 years
Carbamazepine Tablets	2-3 years
Cefixime Tablets	2-3 years
Chlorpheniramine Maleate tablet	2-3 years
Ciprofloxacin Tablets	2-3 years
Cloxacillin Capsules	2-3 years
Cotrimoxazole Tablets	3-4 years
Esomeprazole Tablets	2-3 years
Losartan Tablets	2-3 years
Metformin Hydrochloride Tablets	2-3 years
Metronidazole Tablets	3-4 years
Ofloxacin Tablets	2-4 years
Paracetamol Tablets	2-4 years

The above table depicts the differences in self-life claim among the different brands of same generics. Maximum of 2 years differences were found.

Table 15: Pharmacopoeias standard of tested samples

Items by Pharmacopoeial standard (n=214)	Number	Percentage (%)
United States Pharmacopoeia (USP)	24	11.2
Not mentioned (Non-pharmacopoeial)	63	29.4
Indian Pharmacopoeia (IP)	108	50.5
British Pharmacopoeia (BP)	19	8.9

The above table illustrates tested samples that followed different pharmacopoeial standards. However, 29 % of drug samples did not mentioned which pharmacopoeial standard they had followed.

Table 16: List of substandard drugs

S.N.	Substandard drugs	Brand name	Batch no.	Manufacturer	Remarks
1	Metronidazole Tablets 400 mg BP	Metro-400	MTT-0914	Lomus Pharmaceuticals Pvt. Ltd	GoN
2	Esomeprazole Magnesium Tablets 40 mg	Emez 40	TEZS-106	Alive pharmaceuticals Pvt. Ltd.	Private sectors

3	Ibuprofen Tablets 400 mg IP	Ibuact 400	IB2-077	Vijaydeep Laboratories ltd.	Private sectors
4	Acetaminophen Oral Suspension 125 mg/5 ml USP	Alice P	BEAP 127	Ind-Swift Limited	Private sectors
5	Tamsulosin Hydrochloride Modified Release Capsules 0.4 mg	Flopress-0.4	FP4-09	Nova Genetica Pvt. Ltd.	Private sectors
6	Silver Sulfadiazine & Chlorhexidine Gluconate Cream IP 1%w/w+0.20%w/w	Silver Chlor	FSC5 52	Arya pharma lab Pvt. Ltd.	Private sectors
7	Paracetamol Tablets 500 mg BP	Cetophen	CT-0314	Lomus Pharmaceuticals Pvt. Ltd	GoN
8	Digoxin tablet 0.25 mg	Digicard 0.25	15CQ06	Omnica laboratories Pvt. Ltd.	Private sectors
9	Metronidazole Tablets 200 mg BP	Metroleb-200	T-2983	leben laboratories Pvt. Ltd.	GoN

Among total samples supplied to both laboratories, Paracetamol Tablets BP (Cetophen) supplied as essential drug by Government of Nepal failed to meet the required standard in both labs. Other eight drugs (two supplied by GoN and six supplied from private sectors) were tested in one laboratory only and failed in-vitro test.

Chapter 4

Conclusion and Recommendations

4.1 Conclusion

This study demonstrates that substandard drugs are found in Nepalese market. The widely used drug Paracetamol 500 mg BP (Cetophen) supplied as essential medicine by GoN is found substandard. In addition to this, other eight drugs including two essential medicine supplied by GoN and six non-essential drugs supplied by private sectors are also found substandard. There is also lack of compliance with all the regularity requirements of labeling. Similarly, there are large variations in price among drugs of different brands of same generic name. Few variations can also be seen in terms of expiry date. Health facilities have not fulfilled all the criteria of standard storage system of drugs. In addition, few health posts do not even store vaccines in cold chain.

Medicines are prescribed with generic names from majority of health facilities. Among the prescribed drugs, essential drugs are prescribed in highest quantity. Further, only half of the patients are dispensed complete prescribed medicines from health facilities. Also, most of the people who are dispensed medicines lack complete knowledge regarding medicine use.

4.2 Recommendation

- The drug regulatory authority should make a provision for regular assessment of quality of drugs in the market.
- Measures should be taken to regulate the price of pharmaceutical items.
- Training should be given regarding rational use of drugs targeting the prescriber and dispenser.
- Availability of necessary medicines to the patients from health facilities should be ensured.
- To ensure the quality of drug, provision for proper storage of drugs should be made at all health facilities.

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ANNEX I: Exit client prescription record form

Health Facility: **District:** **Patient ID:** **Patient's age:** **Date:**

Patient's Education:

No formal schooling less than Secondary school Bachelor degree completed

Post graduate degree Higher Secondary (10+2)/ PCL Completed Refused to answer

Diagnosis:

Patient History:

Laboratory Investigation:

Drug Pre-scribed	DF	Dose	F	D	DS 0/1	Qty D	F 0/1	T 0/1	D 0/1	Precaution (If any specify)

Supervisor/ Research Assistant: **Signature:**

DS: Drug Supplied ***F: Frequency***

DF: Drug Frequency ***T: Timing***

QD: Quantity dispensed ***D: Duration***

ANNEX II: Questionnaire for health facility in-charge

Facility: **Date:**

Name of respondent: **Health Post In-charge Name:**

Part 1:

1. Can you tell us who is responsible for examination and prescribing medicines?

MBBS doctor	HA	CMA
Staff Nurse	ANM	Others

2. Who examines and prescribe medicines in the absence of him/her?

MBBS doctor	HA	CMA
Staff Nurse	ANM	Others

3. If yes who does dispense medicines?

MBBS doctor	HA	CMA
Staff Nurse	ANM	Pharmacist/Pharmacy assistant
No specific person designated		Others

4. Has the person involved in dispensing taken any training for dispensing and/or inventory management? If yes. Training title and duration……..

Part 2:

1. What is the average number of patient? Per day: ……..Per month:……..
2. Yearly Drug Budget (in Rs.):

   From Government: From NGO/INGO:

   Local Purchase: Other source:

   (verify record as possible)
3. Is there availability of copy of free essential drug list in the health facility? (Observation)

   Yes No

4. Is there availability of Standard Treatment Guideline (STG)? (Observation) Yes No

Is there availability of vaccines?(Observation)

If yes, is the cold chain storage present for the storage of vaccines? Yes No

Person responsible for handling of refrigerator/cold chain equipments?

MBBS doctor HA CMA

Staff Nurse ANM Others

Has the person taken any training for handling of cold chain equipments? If yes. Training title and duration……

5. Is there any temperature recording device for refrigerator/cold chain? (Observation) Yes No

6. Is there any power backup? Yes No

7. Have you ever calibrated your refrigerator? Yes No

If yes, how?

Part 3: Store

1. Person responsible for handling of medicines/inventory management?

Pharmacist/Asst. Pharmacist HA/CMA Store Officer Others

2. Are there any criteria for ordering the medicines? Yes No

If yes, what are those?

Monthly 3 monthly In 6 months

>6 months Ordering not required

3. Place of storage of medicine (Observation)

Cupboard Table Floor Others (Please specify)

4. Method of storage

Random storage Alphabetical orderAccording to therapeutic category
others (Please specify)

6. Are the drugs kept in direct contact with the light? Yes No

If yes, specify

7. Are the drugs protected from moisture? Yes No

If no, specify

8. Is the storage room well ventilated? Yes No

If no, specify

9. Is the room clean of evidence of rodents (bats, rats) or pests? Yes No

11. Is there separate recording for Narcotic and Psychotropic drugs? Yes No

If yes how it is recorded

How often the expiry date is checked? Daily Monthly Weekly Yearly

8. What do you do if the medicine is of short expiry?

Discard the medicine

Separate the medicine

Dumping or destroying

Return back to the supplier

Quick distribution to the patients

Others (Please specify)

9. How the expired drug is disposed?

Incineration

Burring

Others

ANNEX III: Drug samples by generic name

S.N	Generic Name	Lab-I	Lab-II	TOTAL
1	Acetazolamide tab	0	1	1
2	Albendazole tab	3	3	6
3	Amlodipine tab	9	9	18
4	Amoxicillin Capsules	3	3	6
5	Amoxicillin DT	2	2	4
6	Ampicillin & cloxacillin Capsules	0	1	1
7	Atenolol tab	3	3	6
8	Azithromycin suspension	0	1	1
9	Azithromycin tab	9	9	18
10	Cardiac glycosides tab	0	1	1
11	Carbamazepine tab	0	2	2
12	Cefixime Dispersible tab	3	3	6
13	Cefixime tab	5	4	9
14	Chloramphenicol tab	2	2	4
15	Chloroquin Phosphate tab	0	1	1
16	Ciprofloxacin tab	10	10	20
17	Cloxacillin Capsules	4	4	8
18	Cotrimoxazole tab	0	3	3
19	Cotrimoxazole solution	0	1	1
20	Digoxin tab	0	1	1
21	Doxycycline Capsule	0	2	2
22	Esomeprazole tab	4	6	10
23	Ferrous Sulphate & Folic Acid Tablets	2	3	5
24	Frusemide tab	0	1	1
25	Gentamycin inj	0	1	1
26	Hyoscine Butylbromide tab	0	1	1
27	Ibuprofen tab	0	2	2
28	Ibuprofen &paracetamol tab	0	1	1
29	Lidocaine inj	0	2	2
30	Losartan tab	6	6	12
31	Metformin Hydrochloride SR tab	3	2	5
32	Metformin Hydrochloride tab	4	5	9
33	Metronidazole tab	2	3	5
34	Ofloxacin tablets	6	7	13
36	Oxytocin inj	0	1	1
37	Paracetamol tab	5	5	10
38	Paracetamol oral Suspension	0	1	1
39	Phenobarbitone tab	0	1	1
40	Povidone Iodine Solution	0	2	2
41	Ranitidine Hydrochloride Tablets	2	2	4
42	Ranitidine inj	0	1	1

43	Silver Sulfadiazine cream	0	3	3
44	Tamsulosin Hydrochloride	0	4	4
45	Tinidazole tab	0	1	1
	TOTAL	**87**	**127**	**214**

ANNEX –IV

Brands by different pharmacopoeial standard

Generic	Pharmacopoeial standard
Amoxycillin capsule	IP & BP
Amoxycillin DT	IP
Azithromycin tablet	IP, BP, USP & Non-pharmacopoeial
Cefixime DT	IP, USP & Non-pharmacopoeial
Cefixime tablet	IP & USP
Ciprofloxacin tablet	IP & USP
Cloxacillin capsule	IP, BP & Non-pharmacopoeial
Ofloxacin tablet	IP, USP & Non-pharmacopoeial
Silversulfadiazine cream	IP, BP & USP

Nepal Health Research Council (NHRC)
Ramshah Path, Kathmandu, Nepal
Tel : +977-1-4254220
Fax : +977-1-4262469
E-mail : nhrc@nhrc.gov.np
Website : www.nhrc.gov.np