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# Quality of drug in health facilities: A cross-sectional study

Khem Bahadur Karki,[1] Neelam Dhakal,[2] Baburam Humagain,[3] Arpana Pandit,[4] Trishna Acharya,[5] Pradip Gyanwali[2]

[1]Institute of Medicine, Maharajgunj Medical campus, Department of Community medicine, Maharajgunj, Kathmandu, Nepal, [2]Nepal Health Research Council, Ramshahpath, Kathmandu, Nepal, [3]Nepal Health Sector Support Program, Teku, Kathmandu, Nepal, [4]Kochi University of Technology, Kami, Kochi, Japan, [5]University of Maryland School of Pharmacy, Baltimore, Maryland, USA.

## ABSTRACT

**Background:** Poor quality drugs result minor to detrimental effect on human health. The drug should be of standard quality and should be used appropriately in order to meet its therapeutic efficacy. This study aims to assess the quality of drug in Nepal.

**Methods:** A cross sectional study was conducted in randomly selected 88 health facilities in Nepal from 10th April to 30th June 2016. Selective medicines were collected from both private licensed pharmacies and selected public health facilities. Face to face interview with health facility in-charge of selected health facilities was carried out along with the direct observation of the medicine storage room. The collected medicine samples were dispatched to two laboratories for in-vitro analysis. The labels of the collected medicine were analyzed. The obtained data were entered in Epidata version 3.1, cleaned in Microsoft excel 2007 and analyzed in SPSS version 20.

**Results:** Out of 172 brands, nine brands of medicines were found substandard. Information regarding storage conditions, direction for use and category of the drug were lacking in the label of some brands of medicines. Some selected health facilities were found not meeting major requirements for drug storage: protection from sunlight, moisture, heat, well ventilation and proper sanitation.

**Conclusions:** Few drugs were found to be substandard in Nepalese market from both public and private sectors. Adequate labeling and proper storage condition of medicines in health facilities were lacking.

**Keywords:** Drug quality; private pharmacies; public health facilities; substandard drugs.

## INTRODUCTION

Poor-quality of drug which includes substandard, spurious, falsely labeled, falsified and counterfeit (SSFFC)[1] pharmaceutical products can produce detrimental effects on human health.[2,3] The problem of SSFFC medicines is predominantly a Global issue in health and pharmaceutical aerena.[4] Such drugs threaten public health leading to treatment failure, development of drug resistance, and diminishing confidence in health systems.[5] There are evidences showing increase in SSFC medicines and also rise in issues like: antimicrobial resistance, non-communicable diseases and other malignant disease worldwide.[6-12] In Nepal there is a paucity of studies that have assessed the quality of essential drugs that are available freely in health facilities and the drugs that are available in the pharmacies. It is important to assess the quality of drugs as drugs are mostly consumed by the people who lack complete well-being and thus may exert greater impact on individual's health. Thus, this study aimed to assess the quality of drugs available in health facilities and pharmacy of Nepal.

## METHODS

A cross-sectional study was conducted on five development regions of Nepal. From each development region three districts representing the Terai, Hill and Mountain were selected randomly. From the list of total health facilities of selected district, one District Hospital, one Primary Health Care Centre and four Health Posts were chosen randomly. Altogether, 15 District hospitals, 15 Primary health centers and 58 health posts were

**Correspondence:** Neelam Dhakal, Nepal Health Research Council, Ramshahpath, Kathmandu, Nepal. Email: nelam.dhakal123@gmail.com, Phone: +9779845293645.

included in the study. Two health posts were discarded from the list of selected health facilities since they had been upgraded to Primary health center at the time of the study.

To assess the quality of free essential medicines supplied at public health facilities, altogether 19 drug samples list was prepared for each district to collect medicines from selected health facilities comprising ten medicines from district hospital, four medicines from health posts and five medicines from Primary Health center. Drug to be sampled were chosen on the basis of consensus of steering committee based on three criteria namely Biopharmaceuticals Classification System IV (BCS-IV)[13], frequency of prescription and therapeutic category. The ten medicines from each district hospital include: Digoxin 0.25 mg, Silver sulfadiazine 25 mg, Azithromycin 500 mg, Cloxacillin 250 or 500 mg, Carbamazepine 200 mg, Metformin 500 mg, Amlodipine 5 mg, Ciprofloxacin 500 mg, Ibuprofen 400 mg and Povidone Iodine solution. Medicines from Health post include: Paracetamol 500 mg, Cotrimoxazole 480 mg, Iron and Chlorpheniramine maleate. Medicines from Primary Health Center include: Atenolol 50 mg, Ranitidine 150 mg, Amoxicillin 250 mg, Metronidazole 400 mg and Albendazole 400 mg. The drugs listed in the sample list with at least 6 months period for expiry and availability of the drugs in sufficient quantity required for the in-vitro analysis i.e. 130 tabs/caps in case of tablet/capsule and 8 containers or tubes in case of solution or ointment in those particular health facilities were only collected. The medicines were taken in the required quantity needed for in vitro evaluation. In addition to this, Lignocaine 2% injection was collected from every five regional medical stores. Data collection was carried out from 10$^{th}$ April to 30$^{th}$ June 2016. Data collection was carried out through skilled health professionals including pharmacists, nurses and public health professionals. Two days orientation was given to all the enumerators before deploying them to the field.

To assess the quality of drugs from private sectors, sample list of ten generic medicines was prepared. The list of drugs to be sampled was finalized by technical working group based on three criteria i.e. Biopharmaceuticals Classification System IV (BCS-IV), frequency of prescription and therapeutic category. BCS-IV categories include drugs with least oral bioavailability, low solubility and intestinal permeability. Medicines that are used frequently in various illnesses including medicines from different therapeutic categories and belonging to BCS-IV categories were selected. Any available five different brands from each of ten generic medicines were purchased by explaining the objectives of the study to the concerned person from private licensed pharmacies located in the radius not exceeding 100 meters from each selected district hospitals. Collected ten generic medicines were: Esomeprazole 40 mg, Ciprofloxacin 500 mg, Ofloxacin 400 mg, Cloxacillin 500 mg, Metformin 1000 mg, Losartan 50 mg, Cefixime 200 mg, Azithromycin 500 mg, Tamsulosin 0.4 mg and Amlodipine 5 mg. However, all five different brands of medicines were not available in all the selected districts due to geographical variations and available brands were only purchased in some areas.

Similarly, to collect information regarding storage conditions of drugs in selected health facility, face to face interview was taken with health facility in-charge of selected health facility using structured questionnaire. Also, direct observation of storage room for sunlight exposure, temperature, humidity, sanitation, medicine storage and management were carried out using observation checklist. The observation checklist was prepared based on medicines storage guidelines.

All the collected drug samples from both private and public sectors were kept in a zip lock plastic bag with proper label and packed in a cartoon. The collected drug samples were dispatched to two laboratories for in-vitro analysis. The drug samples were subjected to identification test, weight variation, content uniformity, dissolution test, disintegration test, assay, and active ingredient content for in-vitro analysis. The label of the medicines was also analyzed for sufficient content on the label which includes manufacture date, batch number, expiry date, pharmacopeial standard, storage condition, direction for use, category of the drug and any precautions to adopt. Each sample was analyzed based on the pharmacopeial Standards written on the label i.e. either Indian Pharmacopeia or British Pharmacopeia or United States Pharmacopeia.

Data were entered Epidata version 3.1, cleaned on Microsoft excel 2007 and analyzed using the SPSS version 20. Data were presented on number and percentage in tabular form. To ensure the validity of tools, pretesting was carried out in three health facilities of Kathmandu valley.

## RESULTS

In this study, altogether 172 brands of medicines comprising 154 brands collected from private pharmacies and 18 brands collected from governmental health facilities (supplied at free of cost by Government of Nepal) were tested at two laboratories. Out of total tested brands, nine brands i.e. six brands collected from private pharmacies and three brands collected from

government health facilities failed to comply all the required standards. Table 1 illustrates the list of samples that failed to meet the standard criteria. Among the nine brands that failed to comply the required standard, three samples failed dissolution test, two samples failed both dissolution and disintegration test and two samples failed in content of Active Pharmaceutical Ingredient (API) and rest two samples failed in all dissolution test, content uniformity test and content of Active Pharmaceutical Ingredients (API) test. According to WHO, Substandard medicines are authorized medical products that fail to meet either their quality standards or specifications, or both.

Table 1. List of substandard drugs.

| S.N. | Substandard drugs | Remarks |
|---|---|---|
| 1 | Metronidazole Tablets 400 mg BP(G) | Dissolution fail |
| 2 | Esomeprazole Magnesium Tablets 40 mg(P) | Dissolution and Disintegration fail |
| 3 | Ibuprofen Tablets 400 mg IP(P) | Dissolution and Disintegration fail |
| 4 | Acetaminophen Oral Suspension 125 mg/5 ml USP(P) | Content of API fail |
| 5 | Tamsulosin Hydrochloride Modified Release Capsules 0.4 mg(P) | Dissolution, content uniformity and content of API fail |
| 6 | Silver Sulfadiazine & Chlorhexidine Gluconate Cream IP 1%w/w+0.20%w/w (P) | Content of API fail |
| 7 | Paracetamol Tablets 500 mg BP (G) | Dissolution fail |
| 8 | Digoxin tablet 0.25 mg (P) | Content uniformity, Content of API and Dissolution fail |
| 9 | Metronidazole Tablets 200 mg BP (G) | Dissolution fail |

*G - Drugs supplied from Governmental sector, P- Drugs supplied from Private sector*

On analyzing labels of the 172 brands of medicines, all the samples were found to have mentioned manufacture date, expiry date and batch number but information regarding storage conditions, direction for use and category of the drug were lacking in some brands of medicines. In 7 brands, information about storage conditions on their labels was missing. Similarly, 35 brands had not mentioned about information for maintaining cautions, 33 had not mentioned about directions for use and 34 brands had not mentioned about categories of drug they belong to which is demonstrated in percentage in table 3.

Table 2. Regulatory compliance on labeling.

| Regulatory Parameters | Percentage (%)(N=172) |
|---|---|
| Manufacture date mentioned | 100 |
| Expiry date mentioned | 100 |
| Batch number mentioned | 100 |
| Direction for use | 19.2 |
| Caution mentioned | 79.4 |
| Storage condition | 95.8 |
| Samuha not mentioned | 19.6 |

Further, information regarding storage of drugs at different health facilities was obtained through interview with health facility in-charge and direct observation of the storage room based on observation checklist. All the selected health facilities were not found to adopt complete measures for drug storage i.e. protection from sunlight, moisture, heat, well ventilation and proper sanitation which is presented in table 4. Out of 88 health facilities, only 31 % were found to have adopted sunlight protection measures for storing medicines. Likewise, other measures for medicine storage which includes moisture protection, heat protection, well ventilation and sanitation were found to have been followed by 78 %, 94 %, 73% and 75% of health facilities respectively. Moreover, different responses were obtained from different health facilities regarding management of expired drugs which is illustrated in table 5.

Table 3. Drug storage practice in different health facilities.

| Drug storage practice | DH(n=15) | PHC(15) | HP(58) | Total(88) |
|---|---|---|---|---|
| | % | % | % | % |
| Sunlight protection | 33.3 | 13.3 | 34.5 | 30.7 |
| Moisture protection | 66.7 | 86.7 | 79.3 | 78.4 |
| Heat protection | 100 | 93.3 | 93.1 | 94.3 |
| Well ventilation | 60 | 73.3 | 75.9 | 72.7 |
| Sanitation | 53.3 | 80.0 | 79.3 | 75 |

Table 4. Technique used for managing expired drugs at health facilities.

| Practice for expired drug | DH(n=15) | PHC(n=15) | HP(n=58) | Total (N=88) |
|---|---|---|---|---|
| | % | % | % | % |
| 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 |

## DISCUSSION

Among 172 total brands that were tested in laboratories in this study, 5.23% of medicines were found to be substandard. Among the substandard medicines, three brands of medicines were the medicines collected from public health facilities and six brands were the medicines collected from private pharmacies. The three brands of substandard medicines from public sectors were the most commonly used medicines i.e. paracetamol and two brands of metronidazole. Though, this data is lower than the result obtained in a similar study done by Gyanwali et al in Kathmandu valley which identified 32.5 % substandard medicines among 40 brands analyzed;[14] this is still a serious issue as such medicines can cause serious impact on public health. According to Department of Drug Administration, out of 916 samples tested in National medicine laboratory in 2017, 7.2 % did not comply the required pharmacopeial standard.[15] In a similar study carried out by khuluza Fin Malawi, out of 22 samples tested, 27.3% of samples failed to meet the BP-2007 standards for Active Ingredient content.[16] The compromised quality of medicines do not only exacerbate the disease prognosis but also cause greater threat to the health of people. The medicines: paracetamol and metronidazole supplied by government of Nepal at public health facilities being substandard as seen in this study may reduce trust of public towards the free health services. Substandard medicines produces minimal therapeutic effect which might be interpreted as being resistant to particular medicine by physician and might change the medication; thus might contribute as one of the casual factors for emergence of anti-microbial resistance and various life threatening diseases.

The label of medicines should include information such as: manufacture date, batch number, expiry date, storage condition, direction for use, category of the drug, any precautions to adopt.[17] Appropriate labeling is imperative to ensure medication safety in patients whose misinterpretation might result into administration error ultimately affecting the individual's health.[18] It has been found that medicine compliance, differentiation among different products and readability of the contents are directly correlated to medicine labeling.[19] In this study, only three information were found in all 172 brands that were assessed. This signifies the ignorance of manufacturer on quality of labels of the medicines. Moreover, it also reflects the weakness of authoritative body to monitor and control the regulations of such products.

Guidelines for medicine storage prepared by Logistic Management Division then (now Management Division) have clearly indicated 13 points to be considered while storing medicines in any health facilities.[20] On top of them, the major parameters that need to be maintained in medicine storage room of every health facilities include: temperature, humidity, exposure to direct sunlight and heat, well ventilation and sanitation which directly affects the medicine quality. These all parameters which are crucial contributing factors for poor quality of medicines were not found to be maintained in all the selected health facilities. Medicines stored in such conditions would definitely increase likelihood for degradation. Many health facilities do not have sufficient infrastructures and also space for medicine storage; this arrows the necessity to facilitate health facilities with adequate equipment and infrastructures for maintaining proper storage of medicines along with periodic monitoring by the authoritative body.

This study succeeded to assess the quality of medicines available in both public health facilities and private pharmacies in 15 districts of Nepal representing all three geographical regions. However, there were some limitations of this study. This study could not assess the medicine storage condition of private pharmacies, Regional medical stores and Central medical stores. Similarly, this study was conducted before the country stepped into federalism, so data representative to provinces could not be generated.

This study recommends the establishment and effective implementation of stringent policy on drug regulation. Instead of being limited to fulfill medicine demands of the health facilities, Government should shift its focus on supplying qualitative medicines along with other amenities required to retain the quality of the medicines in all the health facilities. The study also highlights the need for regular post-market surveillance test of medicines supplied from both public and private sectors. Likewise, there should be a provision to ensure uniformity in prices of medicine. There should be a separate department or separate unit in the department primarily concerned on regular monitoring and ensuring the drug quality supplied from both public and private sectors. This study suggests necessity for the further study on assessment of drug quality and consumer behavior in Nepal.

## CONCLUSIONS

This study found the existence of substandard drugs in selected health facilties. The storage conditions of medicines in health facilities were found not being adhered to the national guidelines prepared by Logistic Management Division. Similarly, appropriate labeling which is another paramount aspect were also lacking in majority of medicines.

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