DOI: https://doi.org/10.33314/jnhrc.v19i1.3417

Prescribers Perception on Drug Promotional Literatures in A Tertiary Care Hospital in Nepal

Pravin Prasad,¹ Anish Mudvari,¹ Rakesh Ghimire,¹ Naresh Karki,² Dipendra Yadav,¹ Shruti Shah,³ Pradip Gyanwali¹

¹Department of Clinical Pharmacology, Maharajgunj Medical Campus, Maharajgunj, Kathmandu, ²Department of Pharmacology, Lumbini Medical College and Teaching Hospital, Pravas, Palpa, ³Department of Community Medicine, Kathmandu Medical College and Teaching Hospital Pvt. Ltd., Sinamangal, Kathmandu, Nepal

ABSTRACT

Background: Drug promotional literatures can often be misleading and have biased information and can contribute to irrational use of medicines. Thus, it is necessary that prescribers critically analyze the drug promotional literatures presented to them. This study attempts to understand if the prescribers at Tribhuvan University Teaching Hospital are aware about the necessary information that should be present in a drug promotional literature.

Methods: A descriptive cross-sectional study was conducted over six months in which prescribers at Tribhuvan University Teaching Hospital were provided with the self-administered questionnaire and were requested to submit the filled in questionnaire. Prescribers presently working at Tribhuvan University Teaching Hospital, attending out patient department services and had received drug promotional literatures within last six months were included in this study.

Results: During the study, 163 of the received questionnaires met the inclusion criteria and were utilized for analysis. Advertisement, reminder items and others type of drug promotional literatures were commonly received by prescribers included in our study. Higher proportion of faculties (35.29%) preferred reprint type of drug promotional literatures. Most of the participants (47.85%) searched for 5-8 WHO-Ethical Criteria for Medicinal Drug Promotion criteria when referring a drug promotional literature. It was seen that 42.94% of prescribers realised that at least two out of four types of information related to negative attribute of the promoted medicines were missing.

Conclusions: The prescribers with least duration of clinical exposure are more likely to always prescribe the medicines promoted to them. Prescribers were more confident on claims made in drug promotional literatures if they were supported using scientific evidences.

Keywords: Drug promotional literatures; prescriber perception; WHO-ECMDP

INTRODUCTION

Drug Promotional Literatures (DPLs) are easily available, accessible and hence are an important source of drug information. 1 Various studies have reported DPLs having problems like missing information related to negative attributes of the promoted medicine, containing exaggerated claims, filled with inappropriate pictures, etc.²⁻⁴ Prescriptions by physicians are commonly influenced by the information presented in DPLs, at times without appraising them critically.^{5,6} It has been reported that 59.5% physicians believe information in promotional materials mostly influenced their prescriptions.7 It is thus essential that the information presented in DPLs are critically appraised by the prescribers so that they prescribe medicines rationally.8-10

This study aimed to identify if prescribers at Tribhuvan University Teaching Hospital (TUTH) were aware about the components that should be present in DPLs. The study also attempted to identify the influences of citing different scientific literatures to justify the claims made in DPLs.

METHODS

This study was a descriptive cross-sectional study conducted at Tribhuvan University Teaching Hospital (TUTH) over a period of six months (October 2019 to April 2020) after obtaining ethical approval from Institute Review Board. The list of 392 prescribers (medical officer, residents and faculties) working at TUTH during the time of study was obtained from administration of the

Correspondence: Pravin Prasad, Department of Clinical Pharmacology, Maharajgunj Medical Campus, Tribhuvan University, Institute of Medicine, Maharajgunj, Kathmandu. Email: prapsd@iom.edu.np, Phone: +9779849018596

institute and the names were arranged alphabetically (first name, middle name and last name), regardless of their designation and department.

With the prevalence of physicians believing information in promotional materials mostly influenced their prescription to be 59.50% obtained from a previous study,7 the sample size was calculated and adjusted for 20% non-response rate and was found out to be 480. As the population (number of prescribers) were only 392, sample size was further adjusted for finite population and was calculated to be 216. Sampling was done using Proportionate to Population Sampling (PPS) method and thus 11 out of 20 medical officers, 121 out of 220 residents and 84 out of 152 faculties were sampled by simple lottery method.

Prescribers were included in the study if they were currently working at TUTH, IOM and were involved in delivering outpatient services. Prescribers were excluded if they had not received any DPLs in last six months.

The potential participant selected was contacted, was explained about the study in person by the study investigators (PP, RG and DY), and informed written consent was obtained. They were then provided with the study questionnaire sheet and requested to return the filled in questionnaire within three working days. If not received, the participant was given three more working days failing which they were labelled as nonrespondent and were excluded from the study. The data thus collected were coded and entered in Microsoft Excel 2016 and analysed using Statistical Software for Social Sciences (SPSS) version 22.

The independent variables in the study were department of the prescriber, their designation, years of clinical practice, types of DPLs, scientific evidences cited in DPLs. Similarly, the dependent variables in the study were components prescriber looks for in DPLs (Table 1), components prescriber finds missing in DPLs (Table 1) and confidence on claims made in DPLs using scientific evidences. For the purpose of the study, DPLs were classified into five types (Table 2).11

| Table 1. Components of DPLs with their assigned codes. | | | |
|--|---|-----------|--|
| Code | Component | Туре | |
| E1 | The name(s) of the active pharmaceutical ingredient(s) (API) using either international non-proprietary names (INN) or the approved generic name of the drug; | WHO-ECMDP | |

| F2 | The brand name; | WHO-ECMDP | |
|-----|--|---|--|
| | | *************************************** | |
| E3 | Content of the APIs per dosage form or regimen; | WHO-ECMDP | |
| E4 | Name of the other ingredients known to cause problems; | WHO-ECMDP | |
| E5 | Approved therapeutic uses; | WHO-ECMDP | |
| E6 | Dosage form or regimen; | WHO-ECMDP | |
| E7 | Side-effects and major adverse drug reactions; | WHO-ECMDP | |
| E8 | Precautions, contraindications and warnings; | WHO-ECMDP | |
| E9 | Major interactions; | WHO-ECMDP | |
| E10 | Name and address of the manufacturer or distributor; | WHO-ECMDP | |
| E11 | Reference to scientific literature as appropriate | WHO-ECMDP | |
| 01 | Cost of Formulation | Others | |
| 02 | Tables/graphs to represent results | Others | |
| 03 | Statistical terms used | Others | |
| 04 | Pictures | Others | |

| | ation of types of Drug Promotional cheir explanation. ¹¹ |
|------------------------|---|
| Types of DPL | Description |
| Reprint | Printed material presented in a scientific style; may be a reproduction of an article, abstract, or proceeding of a conference; part of a book, journal, or monograph; or previously unpublished internal research. |
| Advertisements | Printed material designed to attract attention to publicize a product, often by highlighting positive attributes. |
| General Information | Printed material that describes a medical condition, answers questions about a disease, or suggests that there may be an available therapy; or describes a medication, instructs in its use, or answers questions about the medication. |
| Correspondence | Printed material in the form of a letter or memo, addressed to a specific person, discussing a drug or disease. |
| Reminder Items | Printed material calling attention to a drug's name with information limited to drug name, dosage form, or price |
| Others | Materials that do not fall into any of the above categories |

RESULT

Of 216 participants approached, 177 returned the filled in questionnaires which resulted in a response rate of 81.94% and were included in the study. Prescribers from nine departments (Internal Medicine, General Practice and Emergency Medicine, Psychiatry, Dermatology, Surgery, Orthopaedics, Pediatrics, Obstetrics and Gynaecology and Ophthalmology) with mean age of 34.38±6.1 participated in the study. Most of the participants in this study were residents (n=109, 61.58%). It was seen that 163 (92.09%) participants had received DPLs in last six months and their responses were utilized for assessment in the study. The duration of involvement of clinical practice by the participants ranged from 0 to 35 years with a mean of 6.86 ± 6.282 .

Majority of the participants were found to always receive advertisement (n=77, 47.24%), reminder items (n=93, 57.06%) and others (n=86, 53.09%) type of DPLs. It was seen that three medical officers who had been involved in clinical practice for less than a year always used to prescribe the promoted medicines to them. With the increase in duration of clinical practice of physicians (medical officers, residents and faculties), the frequency of promoted medicine being prescribed also declined.

Advertisement type of DPL was most preferred by the medical officers (n=8, 80.00%). Similarly, it was seen that most residents (n=65, 63.73%) and faculties (n=32, 64.00%) preferred general information type of DPLs. On further evaluation, when participants were categorized as residents and non-residents (medical officer and faculties combined) and as faculty and nonfaculty (medical officers and residents combined), it was seen that difference in the preferred type of DPLs was statistically significant for all types of DPLs except for general information type and others type of DPLs (Table 3).

To access the awareness among participants about the necessary components of DPLs, the list of components suggested by WHO-ECMDP was utilized. It was seen that most of the prescribers (n=152, 93.25%) looked for brand names of the promoted medicine (coded as E2) when going through a DPL (Figure 1). Additionally, few other components were also asked about. It was seen that 66.87% of participants looked for pictures present in DPLs. It was seen that higher proportion of participants (n=78, 47.85%) looked for 5-8 criteria as per WHO-ECMDP. A small proportion of participants (n=17, 10.43%) were found to look for 9-11 criteria as listed by WHO-ECMDP. It was further seen that four respondents looked for all 11 criteria listed by WHO-ECMDP.

It was seen that most of the prescribers (n=127, 77.91%) identified that DPLs had "side effects and major adverse drug reactions" (coded as component E7) missing (Figure

| Table 3. Preference of residents); only signific | | non-residents and faculty vs no | on-faculty (medical (| officers and |
|--|-------------|---------------------------------|-----------------------|--------------|
| Type of DPL | Designation | No (%) | Yes (%) | p-value |
| Reprints | Resident | 91 (89.22) | 11 (10.78) | 0.001* |
| | Others | 41 (67.21) | 20 (32.79) | |
| Advertisements | Resident | 43 (42.16) | 59 (57.84) | 0.007* |
| | Others | 39 (63.93) | 22 (36.07) | |
| Correspondence | Resident | 102 (100.00) | 0 (0.00) | 0.001* |
| | Others | 55 (90.16) | 6 (9.84) | |
| Reminder items | Resident | 52 (50.98) | 50 (49.02) | 0.008* |
| | Others | 44 (72.13) | 17 (27.87) | |
| Reprints | Faculty | 33 (64.71) | 18 (35.29) | 0.000* |
| | Others | 99 (88.39) | 13 (11.61) | |
| Advertisements | Faculty | 37 (72.55) | 14 (27.45) | 0.000* |
| | Others | 45 (40.18) | 67 (59.82) | |
| Correspondence | Faculty | 45 (88.24) | 6 (11.76) | 0.000* |
| | Others | 112 (100.00) | 0 (0.00) | |
| Reminder items | Faculty | 37 (72.55) | 14 (27.45) | 0.017* |
| | Others | 59 (52.68) | 53 (47.32) | |

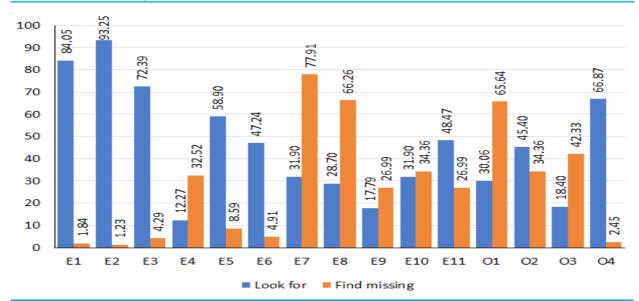


Figure 1. Components in DPLs that participants looked for and components in DPLs that participants found missing while going through DPLs.

Table 4.Level of confidence gained by prescribers if claims in DPLs have different types of references (as classified by SIGN) cited.

| Reference Category | Not applicable | Does not effect | Confident | Very Confident | Extremely confident | Total |
|-----------------------|----------------|-----------------|------------|----------------|---------------------|-------|
| 1++ | 7 (4.32) | 16 (9.88) | 19 (11.73) | 40 (24.69) | 80 (49.38) | 162 |
| 1+ | 7 (4.29) | 18 (11.04) | 26 (15.95) | 44 (26.99) | 68 (41.72) | 163 |
| 1- | 10 (6.13) | 22 (13.50) | 25 (15.34) | 54 (33.13) | 52 (31.90) | 163 |
| 2++ | 8 (4.91) | 15 (9.20) | 40 (24.54) | 55 (33.74) | 45 (27.61) | 163 |
| 2+ | 9 (5.52) | 29 (17.79) | 62 (38.04) | 47 (28.83) | 16 (9.82) | 163 |
| 2- | 15 (9.26) | 37 (22.84) | 62 (38.27) | 35 (21.60) | 13 (8.02) | 162 |
| 3 | 19 (11.66) | 48 (29.45) | 62 (38.04) | 21 (12.88) | 13 (7.98) | 163 |
| 4 | 29 (17.79 | 62 (38.04) | 52 (31.90) | 10 (6.13) | 10 (6.13) | 163 |

Prescribers were also assessed whether they looked for negative attributes (coded as E4, E7, E8 and E9) of the promoted medicine in DPLs. It was found that most of the participants (n=99, 60.74%) did not look for information related to these negative attributes. It was further seen that 11 out of 163 participants included in the study looked for all four negative attributes (coded as E4, E7, E8 and E9) in a DPL. It was also noted that 118 (72.39%) out of 163 participants identified that at least two of these four types (coded as E4, E7, E8 and E9) of information are missing in DPLs.

The citation of scientific evidences to justify a claim made in DPLs was found to influence the confidence of prescribers on the claims. In our study, almost half of the prescribers (80, 49.38%) felt extremely confident if references that are categorised as "1++" (like high quality meta-analyses, systematic reviews of randomised control trials (RCTs), or RCTs with a very low risk of bias) by Scottish Intercollegiate Guidelines Network (SIGN)

category were used to justify claims made in DPL. Similarly, citation of expert opinion (categorised as level 4 according to SIGN category) to justify the claims made in DPL had no effect on the confidence of majority of prescribers (n=62, 38.04%) (Table 4).

DISCUSSION

In our study, it was seen that most of the participants were residents and the mean age of the participants was 34.38±6.1. This could have resulted due to higher number of residents working (220 residents out of 392 prescribers) at this institute. As the sampling was done using PPS method, this also resulted in higher number of residents being included (102 out of 177) in the study. The mean duration of clinical practice was also found to be 6.86 ± 6.282 years, which again could have resulted due to higher number of residents included in the study. The percentage of filled in questionnaire received was found to be 81.94%. Similar response rate has been

reported by a different studies conducted in India.^{7,10}

It was seen that advertisement type, reminder items type and others type of DPLs were commonly received by prescribers in our study. Styrer et al. also reported that advertisement type of DPL was most commonly distributed to physicians.11 In another study conducted in Nepal, it was reported that advertisement type of DPLs were most commonly received. 4 As advertisement type, reminder items type and others type of DPLs are easier to design, focuses on the positive attributes of the medicine being promoted, this could have resulted in most of the prescribers always receiving these DPLs.

Prescribers in our study were found mostly to prefer advertisement type of DPL which has also been reported by another study. Similar to our finding, a study from India reported that brochures were considered as most useful by 33% physicians. The study further reported that advertisement in journals (which has been included in others type of DPLs in our study) were found most useful by 25% of physicians included in the study. 10 Even though advertisements published in well-known journals might not be screened rigorously, their mere presence should not earn confidence of the prescribers on the drug being promoted without its critical evaluation.12

It was seen in our study that all of the young prescribers prescribed the promoted medicine to them, which declined with the increase in the duration of clinical practice. In a study conducted in India, it was reported that 59.5% of prescribers agreed that their prescription practice is mostly influenced by DPLs.7 It has been reported that physicians often miss the fact that they are being influenced by the promotional activities as well as materials.13 It has been reported that 99 out of 182 (54%) of DPLs distributed by pharmaceutical company at residency programme institute were reprint type, 104 out of 238 (44%) and 28 out of 66 (42%) of DPLs distributed at health maintenance office and internists office were of advertisement type respectively. 11 Undergraduate Pharmacology curricula for medical doctors offered by Tribhuvan University does not include activities to help them develop skills to critically analyse DPLs. 14 A study conducted by Giri et. al. in 2005 stated that academic activities like critical analysis of promotional materials and drug advertisements using WHO-ECMDP criteria has been conducted at their institute and students are also evaluated in this regard during their Pharmacology practical examinations.¹⁵ Thus, the young prescribers could have been lured with the claims and attractiveness of the DPLs that have led them to always prescribe the promoted medicine to them.

It was seen that most of the participants in our study

looked for generic name, brand name, and content of active ingredient per dosage form (coded as E1, E2 and E3 respectively) when looking at DPLs. A majority of the participants (66.87%) in our study were found to look for pictures used in DPLs. Pictures are commonly used to make the promotional materials attractive and as a technique of persuasive communication.¹⁶ Drug advertisements studied by Jha et al reported that 16.67% of DPLs containing pictures were irrelevant to the promoted medicine.17 Two different studies from India reported higher proportion of DPLs containing irrelevant pictures.^{2, 16} Such pictures can contribute to prescribing problems like polypharmacy and over-prescription of antimicrobials which has previously been reported to be prevalent in Nepal.18

It was seen that most of the prescribers (n=127, 77.91%) identified that DPLs had "side effects and major adverse drug reactions (ADRs)" (coded as component E7) missing. In a study conducted in Nepal, it was seen that side effects and major ADRs were present only in 33.33% of advertisement type of DPLs studied. 19 Another study conducted by Jha et al. reported that only four out of 100 DPLs studied had this information mentioned. 17 A study reported that physicians commonly find adverse event profile of the promoted medicine is missing in the DPLs. The study also reports that information regarding price of promoted medicine is also commonly missing in DPLs.7 Making misleading or false advertisement related to use, utility or efficacy of any drug in Nepal is deemed punishable as per the Drug Act 1978 AD of Nepal and Department of Drug Administration (DDA) has been authorised to implement the act. 20 Based on WHO-ECMDP, DDA had drafted drug promotional guideline for Nepal in 2007 AD,²¹ however, it gathered lots of resistance and criticism from different stakeholders.22

It was seen that the level of confidence of prescribers was affected if the claims made in DPLs were backed up using scientific studies. This effect in level of confidence of prescribers was also affected by the type of references cited. Another study reporting physicians considering RCTs and meta-analysis as most significant type of references cited in DPLs exists.7 Citation of reference to justify the claims made in DPLs is to earn credibility but there is a common practice by pharmaceutical companies to cite a very large number of unpublished data or a file. Phoolgen et al. reported that due to issues with the references cited in DPLs like ambiguous presentation, questionable retrievability and poor quality, it was difficult to accept the references used in DPLs to support the claims.²³ In another study conducted in USA, it was reported that 75% of the studies cited as reference in DPLs were found to be valid.24

We did not assess if the prescribers verified the scientific evidences cited in DPLs while critically analysing the claims made in DPLs. It would also have been desirable to plan an intervention and check for the change in behaviour of prescribers immediately, over short and long term.

CONCLUSIONS

It was seen that prescribers were receiving DPLs that mainly highlighted the positive aspects of the promoted medicine at TUTH. The duration of clinical practice was found to influence the prescription of the promoted medicine by the prescribers. Even though prescribers looked for most of the criteria suggested by WHO-ECMDP in DPLs presented to them, absence of negative attributes of the promoted medicine was often missed by them. It was also seen that citation of scientific evidences to support the claims in DPLs made prescribers more confident about it.

We would like to recommend for conduct of targeted educational interventions at multiple levels (inclusion of relevant activities in undergraduate curriculum, continued medical education, in-service education, etc) to create awareness and help them develop skill to critically analyse DPLs.

SOURCE OF FUNDING

This study was awarded with Tribhuvan University Mini-Research Grant 2076 (2020 AD).

REFERENCES

- 1. Jadav S, Dumatar C, Dikshit R. Drug promotional literatures (DPLs) evaluation as per World Health Organization (WHO) criteria. J App Pharm Sci. 2014;4:84-8. Available from: http://www.japsonline. com/admin/php/uploads/1270_pdf.pdf
- 2. Ganashree P, Bhuvana K, Sarala N. Critical review of drug promotional literature using the World Health Organization guidelines. J Res Pharm Pract. 2016;5(3):162-5. [PubMed]
- 3. Mikhael EM. Evaluating the reliability and accuracy of the promotional brochures for the generic pharmaceutical companies in Iraq using World Health Organization guidelines. J Pharm Bioallied Sci. 2015;7(1):65-8. [PubMed]
- 4. Prasad P, Bajracharya SR, Deo S, Lamichhane S, Pradhan PMS, Ghimire R, et al. Adherence of drug promotional literatures distributed by pharmaceutical companies to World Health Organization Ethical Criteria for Medicinal Drug Promotion. J Nepal Health Res Counc.

2019;17(3):345-50. [INHRC]

- Khakhkhar T, Mehta M, Shah R, Sharma D. Evaluation of drug promotional literatures using WHO guidelines. J Pharm Negat Results. 2013;4(1):33-8. Available from: http://www.pnrjournal.com/article.asp?issn=0976-9234;year=2013;volume=4;issue=1;spage=33;epage=3 8;aulast=Khakhkhar
- Gopalkrishnan S, Murali R. India: Campaign to tackle unethical promotion. Essent Drugs Monit. 2002;31:22. Available from: https://digicollections.net/ medicinedocs/printable-s4937e.8.9#d/s4937e.8.9
- Chitnis K, Limaye A, Bhosale M. Pharmaceutical promotional literature: opinions of physicians in a tertiary care hospital in Mumbai. Int J Basic Clin Pharmacol. 2013;2(5):541-47. [Article]
- 8. Rohra DK, Gilani AH, Memon IK, Perven G, Khan MT, Zafar H, et al. Critical evaluation of the claims made by pharmaceutical companies in drug promotional material in Pakistan. J Pharm Pharmaceut Sci. 2006;9(1):50-9. Available from: https://ecommons.aku.edu/cgi/ viewcontent.cgi?article=1441&context=pakistan_fhs_
- 9. Jain V, Kaore S, Amane H, Jain M, Katakwar M, Thawani V. Evaluation of rationality of printed promotional medicine literature. International Journal of Health & Allied Sciences. 2016;5(1):45-9. [Google Scholar]
- 10. Sharma S, Akhoon N, Moe HW, Nair DR, Shashidhar V. A study of perceptions and exposure of drug promotional literature among clinicians in a teaching hospital. Perspect Clin Res [Epub ahead of print] [cited 2021 Feb 16]. Available from: https://www.picronline.org/ preprintarticle.asp?id=283866
- 11. Stryer D, Bero LA. Characteristics of materials distributed by drug companies. J Gen Intern Med. 1996;11(10):575-83. [Article]
- 12. Villanueva P, Peiró S, Librero J, Pereiró I. Accuracy of pharmaceutical advertisements in medical journals. The Lancet. 2003;361(9351):27-32.[Article]
- 13. Holloway K, Green T. Drug and the rapeutic committees—A practical guide. Geneva: World Health Organisation; 2003. Available from: http://www.who.int/medicines/library/ par/who-edm-par-2004 1/WHO EDM PAR 2004 1 Drugs and therapeutics committees.pdf. Accessed 28 <u>June 2005</u>.
- 14. Tribhuvan University. Curriculum for Bachelor of Medicine & Bachelor of Surgery (MBBS). Kathmandu:

- Tribhuvan University; 2008.
- 15. Giri BR, Shankar PR. Learning how drug companies promote medicines in Nepal. PLoS Med. 2005 Aug;2(8):710-1.[PubMed]
- 16. Mali SN, Dudhgaonkar S, Bachewar NP. Evaluation of rationality of promotional drug literature using World Health Organization guidelines. Indian J Pharmacol. 2010;42(5):267-72.[PubMed]
- 17. Jha N, Sapkota Y, Shankar PR. Critical Evaluation of Drug Advertisements in a Medical College in Lalitpur, Nepal. J Multidiscip Healthc. 2020;13:717-25. [PubMed]
- 18. Aryal, A., Dahal, A. and Shrestha, R. Study on drug use pattern in primary healthcare centers of Kathmandu valley. SAGE Open Med. 2020;8:1-7.[Article]
- 19. Alam K, Shah AK, Ojha P, Palaian S, Shankar PR. Evaluation of drug promotional materials in a hospital setting in Nepal. South Med Rev. 2009 Apr;2(1):2-6. [PubMed]

- 20. Department of Drug Administration. Drug Act [statute on the internet] Nepal: Ministry of Health,; 1978 [cited 2020]. Available from: http://www.lawcommission.gov.np/en/ wp-content/uploads/2018/10/drugs-act-2035-1978.pdf
- 21. Harper I, Rawal N, Subedi M. Disputing distribution: ethics and pharmaceutical regulation in Nepal. Studies Nepali Hist Soc. 2011;16(1):1-39.[Download PDF]
- 22. Subedi M. Trade in Health Service: Unfair Competition of Pharmaceutical Products in Nepal. Dhaulagiri Journal of Sociology and Anthropology. 2009;3:123-42. [Article]
- 23. Sah P, Sah AK, Jha RK. Evaluation of the rationality of psychotropic drug promotional literatures in Nepal. J Drug Deliv Ther. 2012;2(6):6-8.[Article]
- 24. Cardarelli R, Licciardone JC, Taylor LG. A cross-sectional evidence-based review of pharmaceutical promotional marketing brochures and their underlying studies: Is what they tell us important and true? BMC Fam Pract. 2006;7(1):13. [Article]