



Relevance of pharmacoepidemiology to Nepal

Santosh Thapa¹, Subish Palaian^{1,2}, Hisham Aljadhey³, Pathiyil Ravi Shankar⁴

1. Department of Hospital and Clinical Pharmacy, College of Medical Sciences, Bharatpur, Chitwan, Nepal

2. Department of Pharmacology, College of Medical Sciences, Bharatpur, Chitwan, Nepal

3. College of Pharmacy, King Saud University, Riyadh, Kingdom of Saudi Arabia

4. Department of Pharmacology, Xavier University School of Medicine, Aruba, Dutch Caribbean

BRIEF REPORT

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Corresponding Author:

Santosh Thapa
Department of Hospital and Clinical Pharmacy
College of Medical Sciences, P. O. Box: 23,
Bharatpur, Chitwan, Nepal
[Email: santoshthapachettri@gmail.com](mailto:santoshthapachettri@gmail.com)

Abstract

Drug-related problems such as overuse of injectable drug products and antimicrobials, increased cost of drug therapy, polypharmacy, and adverse drug reactions (ADRs) are prevalent in the healthcare settings of Nepal. To date, no new drug development processes or clinical trials have been conducted in Nepal, despite the fact that studies of real life situations are an essential tool for monitoring medicine use. Pharmacoepidemiology (PE) is an important area that evaluates the effects of drug use in large populations.

Data obtained from pharmacoepidemiological studies may highlight ways to reduce certain drug-related problems and provide reliable information on the safety profile of a drug. Moreover, clinicians and regulatory authorities may also use the data to make drug therapy decisions, drug regulation and policy development. Therefore, there is a great need to conduct appropriate pharmacoepidemiological studies that involve multiple regions and in various groups of the population of Nepal, to collect unbiased and reliable information on drug use.

Key Words

Clinical decisions, drug regulation, Nepal, pharmacoepidemiology

What this study adds

1. Data obtained from pharmacoepidemiological studies can provide information about drug use patterns and ADRs in health institutions and the community and promote the rational use of medicines.
2. The present study provides information about selected pharmacoepidemiological studies in Nepal, the approach to pharmacoepidemiological research in the country and expected outcomes of this research.
3. Pharmacoepidemiology has the potential to provide important data about drug use and ADRs in Nepal with important implications for drug use policies and can promote safer and more rational use of medicines by healthcare providers.

Introduction

Nepal is a landlocked developing country in south Asia, bordered by India and China. Currently, new drug development processes and clinical trials are not being conducted in Nepal. The genetic variations among the population of Nepal are likely to produce more distinct effects than those observed among people involved in the current clinical trials. Overuse of injectable drug products and antimicrobials, ADRs, drug interactions and dispensing drugs to pregnant or lactating women without taking a proper history are some of the drug-related problems that are evident in Nepal.¹⁻⁴

Pharmacoepidemiology (PE) deals with the study of drug effects in a large number of individuals and populations. It applies concepts from clinical pharmacology and epidemiological principles to study the effects of drugs over



time, thereby forming a bridge between clinical pharmacology and epidemiology. PE has been defined as "the study of the use of and the effects of drugs in large numbers of people with the purpose of supporting a rational and thereby cost effective use of safe and effective drugs in the population".⁵ PE can supplement information obtained from premarketing studies, provide information about previously undetected adverse drug effects, study the patterns of drug use, provide information about the economic aspects of drug use and reassurances about drug safety.⁶ The concept of PE was first introduced in the 1960s following an increased emphasis on drug safety and prescribing practices due to the significant adverse effects that restricted the use of drugs like thalidomide.⁷ This concept has since evolved to be a tool for monitoring real world situations such as after drugs are marketed for use.⁸ The application of PE is important in health systems and has been beneficial in reducing drug-related problems in areas of use, as well as in the approval and ultimately for the promotion of rational use of drugs. Developing nations like Nepal have not fully utilised the potential contributions of PE in healthcare settings.⁹ For example, PE studies can aid in the establishment of guidelines in hospitals and also at national level in promoting the rational use of drugs.

Pharmaceutical companies are increasingly involved in pharmacoepidemiologic studies. These companies form alliances with doctors and patient groups and fund studies which exaggerate disease prevalence estimates to show a condition as severe and widespread and requiring treatment.¹⁰ This has been seen in conditions of erectile dysfunction and bipolar disorder in children. Aggressive pharmaceutical promotion has led to disease mongering wherein common ailments are turned into medical problems which create huge profits for the industry but an economic burden at individual and community level.¹¹ Companies have suppressed ADRs of their drug products and exaggerated ADRs of competitor products. A recently published study states that cumulative pooled analysis of all randomised, placebo-controlled trials demonstrated a trend toward increased cardiovascular risk associated with the selective COX-2 inhibitor, rofecoxib compared with placebo as early as December 2000, and the comparison reached a *P* value of 0.05 by June 2001, nearly 3.5 years before the manufacturer's voluntary withdrawal of the drug from the market.¹² Clinical trials with the involvement of pharmaceutical companies often present the therapeutic benefit of a drug positively and fail to mention risks. Published trial results are used by professional medical bodies to construct evidence-based guidelines, so their recommendations may be flawed. This may contribute

to excessive prescription of expensive new drugs whose efficacy is overestimated and risks underestimated.¹³

Selected pharmacoepidemiological studies in Nepal

A Google scholar search (www.scholar.google.com) using the search words (Pharmacoepidemiology, Nepal) and a manual search of existing journals from the institutional library were done during the second and third week of March. The selected articles were discussed among the authors regarding their inclusion in relevant PE studies mentioned in Table 1. The selected PE studies also include the articles obtained during a PubMed search using the search words (Nepal, Pharmacoepidemiology). Priority for selecting relevant studies was given to original articles followed by review articles and short communications.

Most of the PE studies done in Nepal are based on prescribing and drug utilisation patterns and cover almost all of the departments of a hospital as shown in Table 1. The PE studies address various drug-related problems like prescribing antibiotics without indication, overuse of analgesics, antibiotics and expensive nutritional supplements etc. present in healthcare settings of Nepal. This highlights the need for more PE studies to identify the problems and understand the best methods to manage it for better health outcomes. Most studies mentioned here were conducted in a particular region of the country, which means that the results cannot be applied to the whole country. Additional representative studies of more hospitals throughout multiple regions of the country are still needed.

Approach to pharmacoepidemiological research in Nepal

The presence of computerised databases that link the data on the use of medicines and patient medical outcomes are still lacking in Nepal and researchers have to rely on paper medical records. Although some hospital pharmacies use software that provides data on drug use, most of them do not provide clinical information for the patients.

Pharmacovigilance, a sub discipline of PE where a suspected adverse drug reaction is reported by healthcare providers, was first introduced in Nepal in 2004 after the Department of Drug Administration (DDA) the drug regulatory body was nominated as the national centre, working closely with the WHO Collaborating Centre for ADR Monitoring in Uppsala, Sweden.¹⁴ Since then, a number of ADRs have been reported by different centres in the country. This has provided effective data to conduct PE studies in Nepal. Still, this sector lacks adequate co-operation and support from physicians and pharmaceutical companies. In addition, like other developing countries, Nepal lacks qualified personnel,



efficient networking between hospitals, and awareness among the general public regarding pharmacovigilance.¹⁵

Expected outcomes of pharmacoepidemiological research in Nepal

Pharmacovigilance can provide data on the safety profile of drugs and based on this information decisions can be made that supports the protection of human subjects.¹⁶ In Nepal, the incorporation of PE studies along with the collection of pharmacovigilance data can be used to estimate the prevalence and incidence of adverse effect and hypothesis testing, as well as inform the decision making process on drug withdrawal. The regulatory authority of Nepal, the DDA can make necessary decisions whether or not to approve a particular drug for use from the evidence based data available from PE studies done within Nepal.¹⁷ Furthermore, PE studies conducted in Nepal may yield use and effect patterns for drugs that can serve as the basis for formulating a drug list and guidelines at local or national levels. Findings from the PE studies may also provide an idea of antibiotic susceptibility, which helps in framing the local and national treatment guidelines for promoting rational use of medicines.

The presence of sound-alike look-alike medicines, use of abbreviations, improper selection of administration devices are the common problems in hospitals of Nepal and may cause medication errors.¹⁸ In order to study the occurrence and for future prevention of medication errors, PE studies in Nepal would incorporate the good medical record systems, computerised pharmacy systems and data record systems to link these errors with clinical information of the patient.¹⁹ In addition, PE studies would provide insight into the trends of drug use in a particular hospital and region, which would then support the estimation of drug consumption for a defined period of time. The unbiased and valid information provided by PE studies can be successful in providing the health professional with the best level of evidence for making drug therapy decisions. This would ultimately contribute to an overall improvement of health outcomes.²⁰

Conclusion

PE is a new, emerging area in the medical field that takes lessons from real life. It brings about changes in healthcare settings by providing valid and reliable data that can lead to improvements in the present treatment strategies and new treatment approaches for better health outcomes. Nepal can benefit greatly from the application of PE, which can provide data that support changes in policy development, regulation and decisions on drug-related issues.

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PEER REVIEW

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

**Table 1: Selected pharmacoepidemiological studies in Nepal**

S. No.	Author (s)	Objective	Method	Findings
1	Das B et al, 2003 ²⁰	To gain knowledge on drug use during pregnancy	Random once weekly survey of prescriptions of pregnant women during a year	Most prescribed drugs were nutritional supplements like iron, folate, calcium, vitamins. Average number of drugs per prescription was 2.
2	Joshi MP et al, 1997 ²	To study prescribing patterns in geriatric patients	100 randomly selected prescriptions of geriatric patients admitted during a year were analysed	73% of the patients received more than five drugs. IV fluids were the most prescribed drugs (91%) with antibiotics being the second.
3	Sarkar C et al, 2004 ²¹	To determine pattern of drug utilisation of analgesics in dental outpatients	Random once weekly survey of prescriptions of a year was done	74% of the prescriptions contained analgesics. Ibuprofen (41%) and paracetamol + propoxyphene (56%) were the most prescribed non-opioid and opioid analgesic respectively.
4	Wachter DA et al, 1999 ³	To study dispensing of antibiotics by community pharmacies	100 randomly selected prescriptions in two months were studied	97% of the community pharmacies dispensed unnecessary antibiotics for diarrhea. Most of them lack adequate knowledge about disease process and most dispense irrationally.
5	Shankar PR et al, 2005 ²²	To study utilisation patterns of cephalosporins	Case records of admitted patients in inpatient ward during a period of four months were analysed	Cephalosporins were most prescribed in surgery followed by medicine department. Most of them (46.8%) were used for prophylaxis. Cephalosporin utilisation was 4.6 DDDs/100 bed-days.
6	Lamichhane DC et al, 2006 ²³	To study morbidity and prescribing patterns in outpatients	Every 20th patient following the first number chosen among outpatients who visited the OPD during a year were analysed.	Upper respiratory tract infection and acid peptic disease were the most common diagnoses and mean number of drugs used was 1.99. Antihistamines were the most prescribed drug category followed by NSAIDs.
7	Shankar PR et al, 2007 ²⁴	To study prescribing patterns of fluoroquinolones among hospitalised patients	Inpatients enrolled during a period of five months and prescribed with fluoroquinolone were analysed	Fluoroquinolone utilisation was 7.76 DDD/100 bed-days and contributed to 36.7% of the total drug costs and ciprofloxacin was the most prescribed fluoroquinolone.
8	Shankar PR et al, 2010 ⁴	To study drug utilisation in older inpatients	Case records of discharged patients older than 60 years during a year were analysed.	Higher number of drugs especially parenteral and IV fluids were prescribed.
9	Thapa RK et al, 2012 ²⁵	To study the use of antibiotics prophylaxis in Caesarean section	Non-randomly selected women undergoing Caesarean section for a period of three months were analysed	The most prescribed antibiotic was metronidazole (99.5%) followed by ciprofloxacin and gentamicin (50.5% each).
10	Sah AK et al, 2012 ²⁶	To monitor prescribing pattern of NSAIDs in dental outpatients	Randomly selected prescriptions of dental OPD for a period of 6 months were analysed	Ibuprofen + paracetamol (48.4%) was the most prescribed NSAID followed by piroxicam (31%)

IV- Intravenous; DDD- Defined Daily Dose; NSAIDs- Non Steroidal Anti-Inflammatory Drugs; OPD- Out-Patient Department