



REVIEW ARTICLE

Need for involving the pharmaceutical industry in the national pharmacovigilance program of Nepal

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Introduction: Adverse drug reactions (ADRs) have high morbidity and mortality and can cause a significant burden on patients. Most of the data on ADRs are generated from the developed world, and these data cannot be generalized to developing nations due to the variation in prescribing patterns, regulatory policies, and varied effects of drugs. Implementing a successful pharmacovigilance program in many developing countries faces several challenges including under-reporting, human resource shortage, financial challenges as well as poor policy and legal framework.

Method: In this commentary, we aim to explore the situation of Pharmacovigilance in Nepal through a close comparison with India and suggest ways to strengthen the same.

Results: Nepal is still in the beginning stage of Pharmacovigilance and ADR reporting is quite low. The Pharmacovigilance System in Nepal is limited to regional centers which report ADRs to the national center. There is no involvement of pharmaceutical industries in the system which may be a major reason for underreporting and suboptimal functioning of the pharmacovigilance system.

Discussion: Nepal must mandatorily involve pharmaceutical industries in pharmacovigilance. The new drug policy is under revision and addresses aspects of pharmacovigilance in terms of patient safety and the role of pharmaceutical companies.

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Introduction

The World Health Organization defines pharmacovigilance (PV) as 'the pharmacological science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problem' (WHO, 2006). The safety of medicines during normal use and the artificial situation of clinical trials should be carefully monitored to reduce the risks related to drug use and maximize their beneficial effects (Mammi et al., 2013). Adverse drug reactions (ADRs) are an important problem globally. ADRs have high morbidity and mortality and can cause a significant burden on the patients (Pirmohamed et

al., 2004; Davies et al., 2009; Bates et al., 1997). ADRs contribute to a significant number of hospital admissions in different countries. The number of patients admitted to the hospitals due to ADRs accounts for 3-10% or even more of the total admissions (Hamilton et al., 2009; Moore et al., 1998; Griffin JP, 1998). A study from Nepal shows the prevalence of ADRs as 4.61% among hospitalized patients in a tertiary care center (Alam et al., 2014). Drug regulatory authorities have implemented pharmacovigilance to improve medication safety for patients (Mehta et al., 2014). Adverse events have been detected time and again, and many governments worldwide have passed acts and established agencies to monitor these events, identify the



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causes, and mitigate the risks. However, it was the eighteenth World Health Assembly in 1965 that globalized adverse drug reaction monitoring through the establishment of the International Drug monitoring program in 1970 (WHO, 2006).

Most data on adverse drug reactions are generated from the developed world, and these data cannot be generalized to developing countries due to the variations in prescribing patterns, regulatory policies, and the varied effect of drugs. Food and other medicines consumed can also influence the response. The implementation of the Pharmacovigilance program in the developing world is crucial. The program in many developing countries faces challenges like ADR under-reporting, inadequate human resources, shortage of money, as well as poor policy and legal framework.

Method

In this commentary, we aim to explore the situation of Pharmacovigilance in Nepal through a close comparison with India and suggest ways to strengthen the Pharmacovigilance System of Nepal.

Result and Discussion

Context of Pharmacovigilance in India

In India, pharmacovigilance started in 1986 when under the supervision of the Drug Controller of India. India joined the World Health Organization Programme for International Drug Monitoring in 1998. The program was renamed the Pharmacovigilance Programme of India (PvPI) in 2010 by the Ministry of Health and Family Welfare (MoHFW). Indian Pharmacopoeia Commission (IPC) under the MoHFW is the National Coordination Centre (NCC) for PvPI since April 2011 (European Commission, 2014).

As in the case of Nepal, most pharmaceutical industries in India manufacture drugs that have been already approved and marketed in the developed world. This has reduced the urgency to establish a strong indigenous Pharmacovigilance system in both nations. Unlike Nepal, India has moved forward in initiating its Pharmacovigilance System and has incorporated pharmaceutical industries in reporting. India is a growing clinical research hub and the increasing investment of Indian pharmaceutical industries in research and development has led to the development of new drugs.

The Drug and Cosmetics Act 1945 of India was amended in 2005 incorporating provisions relating to pharmacovigilance. The amendment elaborated the obligations in terms of pharmacovigilance of companies planning to develop and/or market new drugs in India. A pharmaceutical company with a marketing license should ensure the establishment of an adequate pharmacovigilance system to monitor the safety of their marketed products, as specified in Schedule Y (CDSCO, 2005). Schedule Y was amended on 20th January 2005, better defining the responsibilities of pharmaceutical companies for their

marketed products as well as those relating to the reporting of adverse events from clinical trials.

Context of Pharmacovigilance in Nepal

Nepal is still in the beginning stage of Pharmacovigilance. The pharmaceutical sector in Nepal is estimated to be worth around 60 billion Nepalese rupees (USD 500 million) in the fiscal year 2020/21 (Dhakal N, 2021). Nepal manufactured NPR 24 billion worth and imported NPR 27 billion worth of medicines in the fiscal year 2019/2020 (Nepal Economic Forum, 2020). The number of domestic pharmaceutical industries registered with the Department of Drug Administration (DDA) is 120, of which 72 are allopathic and 48 are Ayurvedic industries. Out of the 120 pharmaceutical industries, only 36 are Good Manufacturing Practice (GMP) certified companies. Many medicines are imported from foreign companies and there are 400 importers registered with the national drug regulatory authority, the Department of Drug Administration (DDA). DDA was established in 1979 to enforce the Drug Act which was promulgated for the first time in 1978. All the pharmaceutical regulations and policies are regulated by the DDA. There are about 20,000 brands of medicines registered in Nepal. The in-house capacity to manufacture medicines is currently 45%. The current budget allocation for DDA is only 0.5% of the total Ministry of Health and Population budget. Currently, the pharmacy manpower registered with the Nepal Pharmacy Council is around 15000 (Matrix services, 2005).

The promulgation of the Drugs Act in 1978 was the first effort to assuring the safety, quality, and efficacy of drugs in Nepal. The pharmacovigilance program was initiated in Nepal in 2004, with the DDA being designated as the National Center in 2006. DDA is responsible for coordinating with the Uppsala Monitoring Centre, the World Health Organization (WHO) Collaborating Center for International Drug Monitoring. Currently, fifteen regional pharmacovigilance centers are operating and these centers report ADRs to the national center (DDA).

Although there were established Pharmacovigilance centers in Nepal in 2006, there are only 972 ADR reports so far in the national database which reflects the gap in effective implementation of the pharmacovigilance system (DDA, 2022). In about sixteen years, the average number of ADR reports per year is only around 61 which is very low. In the United States, the number of ADRs reported every year through FDA's MedWatch program is around 400,000 (GAO, 2006).

Several studies have explored the reasons for underreporting of ADRs, and the major one is the lack of knowledge and awareness among healthcare professionals (Shrestha et al., 2020). The other reasons are the poor infrastructure of the health system, uncertain supply and doubtful quality of medicines, poor access to healthcare facilities, and lack of collaboration between national

stakeholders, pharmaceutical companies, and healthcare facilities in Pharmacovigilance (Elshafie et al., 2018).

Role of Pharmaceutical companies in Pharmacovigilance

The national Pharmacovigilance System in Nepal is limited to regional centers such as hospitals. There is no involvement of pharmaceutical industries in this system which may be a major reason for underreporting and suboptimal functioning of the pharmacovigilance system in Nepal. Nepal must initiate reporting of ADRs by pharmaceutical industries and make it a mandatory process. To do this, the Drug Act should be revised with the incorporation of Pharmacovigilance activities. Collaboration among various stakeholders, i.e., the Ministry of Health and Population (MoHP), Department of Drug Administration (DDA), Nepal Health Research Council (NHRC), Pharmaceutical Companies, and regional centers should be initiated to develop a robust pharmacovigilance system.

The legislative and regulatory framework in developed nations like the United States, European Union, mandates the pharmaceutical industry to disclose the safety data regarding their products to the regulatory authorities. Pharmacovigilance by a pharmaceutical company comprises two stages - premarketing and postmarketing (Shani et al., 2008). In the premarketing stage, a new drug is required to prove its safety, efficacy, and quality. Pharmaceutical industries are also required to perform post-marketing surveillance of their products to ensure the safety of the medicines after receiving marketing approval. This process is vital for obtaining information about the possible risks of the drugs when they enter the market and are used by a wider population. Any ADRs in this phase should be reported and can sometimes even lead to the product withdrawal from the market. For example, the COX-2 selective inhibitor Rofecoxib.

Conclusion

Pharmaceutical companies should also be involved in the post-marketing surveillance of medicines. Till date, however, not all manufacturers are submitting the post-marketing surveillance (PMS) reports. There is no mandate to submit such reports for manufacturers and importers in Nepal. However, some international pharmaceutical companies are submitting PMS reports. There may be challenges to involving all the pharmaceutical companies in the ADR reporting process as there is no law and regulation till date to address this issue. The new drug policy is under revision and addresses aspects of pharmacovigilance in terms of patient safety and the role of the pharmaceutical companies. Revision of the drug act might enforce ADR reporting from pharmaceutical companies and strengthen Nepal's program. Serious efforts to involve the pharmaceutical industry should be initiated

as soon as possible. The safe use of medicines in Nepal depends on this effort.

Conflicts of Interest

The authors declared no conflict of interest concerning this research work.

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