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Role of Pharmacovigilance Programme of India (Pvpi) in Adverse Drug Event Monitoring for Medication Safety in Patient

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ABSTRACT:
A pharmacovigilance system is a specialized domain within the pharmacological sciences that pertains to the reporting of Adverse Event Reactions associated with medical devices and pharmaceuticals. An adverse event represents a potential public health concern that necessitates continuous documentation, evaluation, and surveillance. Regulatory measures about pharmaceuticals have been enhanced and fortified since the catastrophic sulphanilamide incident of 1937 and the thalidomide tragedy of 1960. In response to these historical events, a Pharmacovigilance System was established, designed to receive, diagnose, assess, monitor, and mitigate the detrimental effects associated with medical products.(1)
The Central Drug Standard Control Organization (CDSCO) oversees the pharmacovigilance framework in India. Within India, the pharmacovigilance initiative is tasked with the oversight of adverse drug responses. India has instituted a comprehensive Pharmacovigilance Program to monitor and document adverse drug reactions. Similarly, the United States has implemented stringent regulations to fortify the pharmacovigilance requirements set forth by the Food & Drug Administration (FDA). The World Health Organization (WHO) has established an International Monitoring System in cooperation with the Uppsala (1–3)Monitoring Centre (UMC).
Improving patient safety and welfare in the Indian population by monitoring drug safety & thereby reducing the risk associated with the use of medicines is the primary mission of the pharmacovigilance program in India. Advocating for safe drug use may become a top focus for the Indian Pharmacopoeia Commission, which also functions as the National Coordination Centre for India's Pharmacovigilance Program. The risk of adverse reactions necessitated the pharmacovigilance system for patient safety. A literature search documented better health literacy of patients through intervention. (3)

KEYWORDS: Pharmacovigilance, Adverse Event Reactions, Drug, Drug safety and efficacy, Drug Monitoring

INTRODUCTION :

Content (Times New Roman front 10) In India, a system is already in place to report adverse events of drugs and vaccines. The Central Drugs Standard Control Organization (CDSCO) started a country- wide Pharmacovigilance program supported by DGHS, Ministry of Health & Family Welfare Government of India. The program was coordinated by the National Pharmacovigilance Centre at CDSCO. The National Pharmacovigilance Advisory Committee supervised the program

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The data collected during these trials help establish the safety profile of a drug. Statistical and epidemiological methods are used to identify potential safety signals from the large volumes of data collected. These signals warrant further investigation to assess the causal relationship between the drug and the adverse event. Once a signal is identified, (2)Pharmacovigilance professionals conduct in-depth assessments to determine the risk-benefit balance of the drug. If necessary, risk minimization strategies, such as label changes or restrictions in use, are implemented. Pharmacovigilance systems allow for the early detection of adverse reactions or safety concerns (1)related to medications. This enables timely interventions and prevents harm to patients. By evaluating and analyzing safety data, pharmacovigilance contributes to the enhancement of drug labeling and prescribing information. This empowers healthcare professionals to make informed decisions and prescribe medications appropriately. It is key to understand the adverse reactions to medicines that are captured in both the clinical and post-market settings. (2)In the pre-approval clinical setting with a medicinal product: all noxious and unintended responses to a medicinal product related to any dose are considered as Adverse Drug Reactions (ADRs). However, Adverse Events (AEs) are any untoward events that occurred during drug therapy administration and have no relation to its use or any untoward medical occurrence in a patient or clinical subject. The difference between an ADR and an Adverse Event (AE) is the harm caused by appropriate or inappropriate use of a drug whereas adverse drug reactions are a subset of these events, where harm is directly caused by a drug under appropriate use (i.e. at normal doses) which defines the causal relationship

Any medicine is said to be safe only when its benefits are greater than the associated risk. With the assistance of PV, the complete safety profile of a marketed medicine/drug is possible with constant and continuous monitoring in a diverse population.(1) During the research and development of a medicine/drug, PV collects data that reflects a drug's safety and effectiveness before submission for marketing.

Some Important Safety Databases(4)

- **VigiBase**: VigiBase is the single largest drug safety data repository in the world Since 1978 the Uppsala Monitoring Centre (UMC; established in Uppsala, Sweden) on behalf of WHO, has been

[i]maintaining VigiBase. Vigibase is used to obtain information about the safety profile of a medicinal product These data are used by pharmaceutical industries, academic institutions, and regulatory authorities for statistical signal detection, updating periodic reports, ICSR comparisons with company databases, and studying the reporting patterns. (4)The data is collected from each of its 110 member states. About a hundred thousand ICSRs are added each year.

- **EudraVigilance**: A centralized European database of suspected adverse reactions to medicines that are authorized or being studied in clinical trials in the European Economic Area The European Medicines Agency (EMA) operates the system on behalf of the European Union (EU) medicines regulatory network.
- **FAERS**: FDA Adverse Event Reporting System: This is a database that contains information on adverse events and medication error reports submitted to the FDA.

Method

This review is based on a comprehensive analysis of existing literature, government reports, and data from the PvPI. A systematic search was conducted using databases such as PubMed, Google Scholar, and the PvPI official website. (4)Keywords included "Pharmacovigilance in India," "PvPI," "Adverse Drug Reactions," and "Drug Safety." Studies and reports published between 2010 and 2024 were included to provide an up-to-date overview of the PvPI's role and challenges.

Why ADR monitoring in India

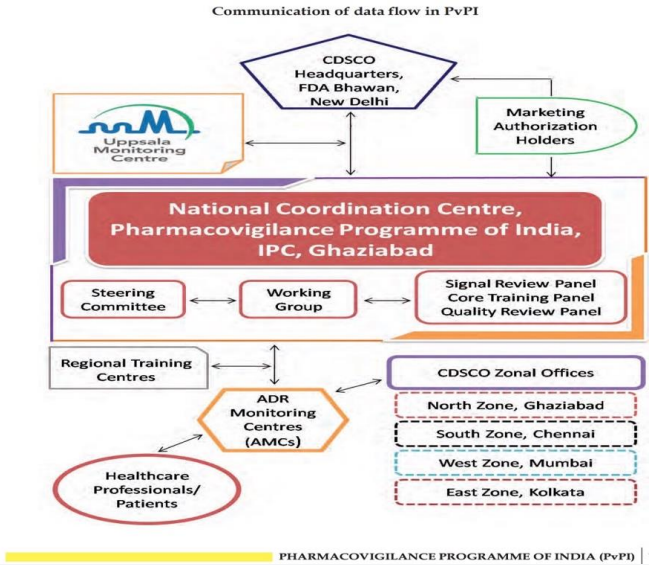
It has been noted that a medication proven effective in a substantial patient population often fails to yield the same results in individuals of varying ancestry. (1)The genetic background of patients plays a crucial role in influencing their response to medications, including factors such as drug targets, drug-metabolizing enzymes, drug transporters, and genes that indirectly affect drug efficacy. These genetic variations can alter drug toxicity and contribute to differences in individual responses.(2) Consequently, adverse drug reactions can differ significantly among individuals, posing a major challenge in drug therapy and development. For instance, pioglitazone is prohibited in certain developed nations due to a heightened risk of bladder cancer, whereas it remains available in India, where the incidence of bladder cancer is lower. Therefore, even if a drug has received approval in one country, it is essential to conduct clinical trials with thorough pharmacovigilance monitoring in populations of diverse races and ethnicities.

Pharmacovigilance Programme in India

The All India Institute of Medical Sciences (AIIMS), New Delhi, was designated the National Coordination Center for the Pharmacovigilance Programme of India (PvPI), established by the Indian government on July 14, 2010, to preserve public health. (2)This Program established 22 ADR monitoring centers, including AIIMS in New Delhi, in 2010. In the year 2024, the India Pharmacopoeia Commission organized a PvPI training program under which the main vision was to safeguard the health of the Indian population by ensuring that the benefits of the use of medicine outweigh the risks associated with its use and the main mission is to improve patient safety and welfare in Indian population by monitoring drug safety & thereby reducing the risk associated with the use of medicines.(3) The main objective of the Program

- To train the various types of participants to develop skills in Pharmacovigilance (PV).
- To build capacity in the area of PV.

- To create awareness & sensitize the participants for reporting of Adverse Events/Adverse Drug Reactions
- To foster research in the area of PV



Pharmacovigilance Methods (4)

Passive surveillance: • encompasses all spontaneous AEFI reporting

- from immunization service providers/hospitals/patients
- up to the next levels: state/territory then national (TGA) and then global Active surveillance:
- primarily used for characterization of the AEFI profile, rates, and risk factors
- logistical and resource constraints limit wide application
- only for selected AEFI at selected institutions (sentinel) sites
- can also be carried out in the community setting (e.g. cohort event monitoring)

Ad hoc studies: • epidemiological studies (e.g. cohort study, case-control study, case series studies) • focus on selected vaccine safety concerns (e.g. testing causality hypotheses) • retrospective or prospective J Pharmacovig Drug Safety Rahman SZ and Galib R: Pharmacovigilance in India Journal of Pharmacovigilance and Drug SafetyVolume 19 | Issue 1 | January – June 2022 16 variety of different species may react very differently to the same medicine. Even within a species, the complex nature of understanding different dosages and different weights for animals, together with changing pharmacokinetics due to age and gender differences, produces its own unique set of challenges apart from human Pharmacovigilance.

Environmental Pharmacovigilance Indian scientist proposed the discipline of Environmental Pharmacovigilance for monitoring adverse events of drugs on other flora and fauna after administration of medicine either in human or animal.[29] This is different than human and veterinary pharmacovigilance. These therapeutic drugs are eliminated into the environment via living organisms.

Environmental Risk Assessment (ERA) if done properly, before the clinical trial may minimize the risk and impact of drugs on environment.[30] This discipline initially was termed as Pharmacoenvironmentology", but later known by other names such as EcoPharmacovigilance, PharmEcovigilance, and

PharmaEcostewarship. Challenges of PV in India J Pharmacovig Drug Safety Rahman SZ and Galib R: Pharmacovigilance in India Journal of Pharmacovigilance and Drug Safety Volume 19 | Issue 1 | January – June 2022 16 variety of different species may react very differently to the same medicine. Even within a species, the complex nature of understanding different dosages and different weights for animals, together with changing pharmacokinetics due to age and gender differences, produces its own unique set of challenges apart from human Pharmacovigilance.

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Challenges of PV in India

The primary obstacle confronting the Pharmacovigilance and Post-Marketing Surveillance (PVPI) is the significant underreporting of adverse drug reactions (ADRs).(3) This issue arises from various factors, including insufficient medical knowledge regarding drug administration, a lack of adequately trained personnel in pharmacovigilance, and a general deficiency in nationwide awareness of pharmacovigilance practices. Additional challenges include outdated infrastructure, prolonged intervals between the establishment of guidelines and legal frameworks, a conservative approach to new drug research, and a scarcity of regulatory inspections related to pharmacovigilance. (4)Moreover, there are instances where ADRs go unrecognized by physicians upon patient admission, potentially leading to fatalities. Patients may also fail to disclose the use of medications from alternative medical systems. The financial burden of ADRs on the healthcare system is substantial. In the marketplace, the introduction of new medications without comprehensive long-term safety evaluations by regulatory bodies has led to increased self-medication among patients, who often transition from prescription-only medications to over-the-counter options, thereby heightening their risk of experiencing ADRs. Historically, India's regulatory agencies and pharmaceutical companies relied on long-term usage experiences for safety assessments. (2)Additionally, the reporting and comprehension of pharmacovigilance concerning traditional medicine systems present unique challenges, as each complementary and traditional medicine employs distinct treatment methodologies based on their theoretical frameworks, such as the principle of drug substitution and issues arising from misidentification due to inadequate knowledge of pharmacognosy

Future Prospects of Pv in India

The system requires enhancement through collaboration between pharmacovigilance (PV) experts and information technology (IT) professionals, leveraging India's advanced IT sector. Given that PV involves managing a significant volume of adverse drug reactions (ADRs), it is prudent for PV specialists to work alongside software developers to create a robust system. The software solutions developed can facilitate the collection and analysis of data sets, identify trends in drug usage across various disease areas, monitor

compliance, address medication errors, and assess drug interactions that may lead to ADRs. Additionally, as clinical research and PV outsourcing activities increasingly take place in India, the Drug Controller General of India (DCGI) needs to invest in a comprehensive PV system. (4)This investment will empower assessors and decision-makers to evaluate safety data and make regulatory decisions independently of other countries. In recent years, numerous Indian companies have ramped up their investments in research and development, enhancing their capabilities to create and market new drugs through their own research initiatives. Once a product is launched, new information will emerge that could influence its benefit-risk profile. (4)A thorough evaluation of this new information generated through PV activities is crucial for all products to ensure their safe usage. Therefore, the DCGI should take decisive actions and commit to enforcing mandatory PV practices while fostering a culture of PV inspections.

The ADR form could be enhanced to be more mobile-friendly, allowing for convenient access as a mobile application. Each medical system has the potential to create its dedicated mobile application. Below are examples of several mobile applications.(2)

1. ADR PvPI mobile application (https://play .goggle.com/store/apps/detail?id=com.vinfotech.suspectedadversedrugreaction&h1=en_In&gl=US)
2. SiddAR Mobile Application ADR form could be developed more mobile friendly as it is easy to carry it as mobile application. Each system of medicine could develop their own mobile application.

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CONCLUSION:

Pharmacovigilance (PV) may influence certain risk factors that contribute to the emergence of specific adverse drug reactions (ADRs).(2) PV needs to expand its focus to include patients as a valuable source of information alongside traditional stakeholders such as healthcare professionals.(4) The Drug Controller General of India (DCGI) must enhance PV practices promptly to integrate Good Pharmacovigilance Practice (GPP) into its processes and strategies, thereby ensuring regulatory consistency and improving both clinical trial safety and post-marketing surveillance. A robust PV system is crucial for the careful use of medications, benefiting medical professionals, regulatory authorities, pharmaceutical companies, and patients alike. (3)It assists pharmaceutical firms in monitoring the safety of their products. (4)Post-marketing PV presents significant challenges and demands considerable effort from regulatory agencies and the entire industry.

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