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International Journal of Current Research in Life Sciences
Vol. 12, No. 10, pp. 3487-3491, October, 2023

ISSN: 2319-9490

REVIEW ARTICLE

A NARRATIVE REVIEW ON ADVERSE DRUG REACTIONS REPORTING: CURRENT PRACTICES AND CHALLENGES

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Received 17th August, 2023; Accepted 27th September, 2023; Published 30th October, 2023

ABSTRACT

The review delves into the existing ADR reporting systems, including the involvement of healthcare professionals and the growing role of patient-driven reporting initiatives. It examines the strengths and weaknesses of these systems and emphasizes the need for enhanced reporting practices to capture a comprehensive range of adverse reactions. Challenges in ADR reporting, such as underreporting, reporting bias, and difficulties in causality assessment, are critically analyzed. The impact of incomplete or inaccurate information on signal detection and risk assessment is also discussed. The review underscores the significance of addressing these challenges to maintain the integrity of pharmacovigilance efforts and optimize patient care. Moreover, the review highlights emerging technologies, including artificial intelligence and real-world data integration, as potential tools to streamline ADR reporting and signal detection processes. These innovations have the potential to revolutionize drug safety surveillance and improve the overall efficiency of pharmacovigilance practices. This narrative review explores the current practices and challenges in adverse drug reactions (ADR) reporting, shedding light on the importance of pharmacovigilance in ensuring patient safety and optimizing drug therapy. Adverse drug reactions represent a critical concern in healthcare, warranting continuous monitoring and evaluation to detect and manage potential risks associated with medications.

Key words: *Adverse Drug Reaction Reporting, Pharmacovigilance, Drug Monitoring, Uppsala Monitoring Centre.*

Citation: Dr. Makarand Gambhire, Sachin Tadge and Dr. Abhijit Kulkarni. 2023. "A narrative review on adverse drug reactions reporting: current practices and challenges" *International Journal of Current Research in Life Sciences*, 12, (10), 3482-3486.

INTRODUCTION

Adverse Drug Reaction: An adverse drug reaction (ADR) refers to any unexpected or harmful response resulting from taking a medication or drug. Also known as adverse drug events (ADEs), these reactions can range from mild side effects to severe, life-threatening complications. ADRs can occur due to various factors, including individual variations in drug metabolism, interactions with other medications or substances, allergies, dosage errors, or underlying health conditions. Some common examples of ADRs include nausea, dizziness, skin rashes, gastrointestinal disturbances, and allergic reactions. In more severe cases, ADRs may lead to organ damage, anaphylaxis, or even death (Al Dweik, 2017). Monitoring and understanding ADRs are crucial in healthcare, as they can impact patient safety and treatment outcomes. Pharmacovigilance, the process of monitoring and evaluating drug safety, plays a significant role in detecting and managing adverse drug reactions. Through pharmacovigilance, healthcare professionals and regulatory authorities can collect and analyze data on ADRs to assess drug safety profiles, update drug labels, and make informed decisions about the continued use of medications (Vivekanandan, 2015). The reporting of adverse drug reactions is essential to identify potential safety issues with medications, ensure patient well-being, and improve overall drug safety. Both healthcare professionals and patients are encouraged to report suspected ADRs to the relevant authorities or healthcare institutions to enhance patient care and contribute to safer medication practices (Matos, 2015).

Pharmacovigilance: Pharmacovigilance, the science, and activities related to the detection, assessment, understanding, and prevention of ADRs, plays a crucial role in monitoring the safety of medications after they are approved for public use (Durrieu, 2016). To improve drug safety and patient care, healthcare professionals and patients are encouraged to report any suspected adverse reactions to the appropriate regulatory authorities or healthcare institutions. Timely and accurate reporting of ADRs contributes to the ongoing evaluation of drug safety profiles and may lead to necessary changes in drug labeling, usage guidelines, or even withdrawal of medications from the market if deemed necessary for patient safety (Waller, 2010).

Historical Background: Pharmacovigilance, the science and practice of monitoring and evaluating the safety of medications, has a rich history that spans several decades. Here is an overview of the key milestones in the history of pharmacovigilance:

Thalidomide Tragedy (Late 1950s - Early 1960s): The thalidomide tragedy stands as a pivotal event in the history of pharmacovigilance. Thalidomide was a drug prescribed to pregnant women for morning sickness and sleeplessness. However, it was later discovered that thalidomide caused severe birth defects, leading to limb deformities in thousands of newborns. This tragic incident highlighted the need for

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rigorous drug safety evaluation and monitoring (van Grootheest, 2003).

Kefauver-Harris Amendment (1962): In response to the thalidomide disaster, the United States passed the Kefauver-Harris Amendment, which strengthened drug regulation and required pharmaceutical companies to demonstrate the efficacy and safety of their products before approval. It also established the requirement for post-marketing surveillance to monitor adverse drug reactions after drugs were on the market (Anderson, 2011).

World Health Organization (WHO) Programme for International Drug Monitoring (1968): The WHO established the Programme for International Drug Monitoring (PIDM) in collaboration with Uppsala Monitoring Centre (UMC) in Sweden. PIDM aimed to collect and analyze information on adverse drug reactions from various countries, fostering international cooperation in drug safety (World Health Organization, 1972).

Development of Adverse Drug Reaction Reporting Systems (1970s - 1980s): During this period, many countries developed their own national adverse drug reaction reporting systems and pharmacovigilance programs. These systems allowed healthcare professionals and the public to report suspected adverse reactions, contributing to a growing database of drug safety information (Kalaiselvan, 2014).

International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) (1990s): The ICH, a global organization comprising regulatory authorities and pharmaceutical industry representatives, was formed to harmonize drug development and regulatory standards. ICH guidelines have since addressed various aspects of pharmacovigilance and safety reporting, streamlining practices on an international scale (Ranganathan, 2003).

Strengthening of Regulatory Oversight (2000s): In the early 2000s, various regulatory agencies around the world, including the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), intensified their efforts to strengthen pharmacovigilance systems. This included implementing risk management plans, enhancing safety labeling, and improving signal detection methods (The Drug Control Department under the Government of the Republic of Lithuania, 2021).

Advancements in Technology (Recent Years): With the advancement of technology, pharmacovigilance has seen significant improvements in data collection, signal detection, and data analysis. The use of electronic health records, data mining techniques, and artificial intelligence has enhanced the efficiency and accuracy of adverse drug reaction monitoring (Fossouo Tagne, 2023).

International overview: Nowadays, adverse drug reactions (ADRs) are a significant global concern in healthcare systems worldwide. ADRs can affect patients of all ages and can occur with various types of medications, including prescription drugs, over-the-counter medications, herbal remedies, and vaccines. Here is an international overview of ADRs (Bandekar, 2010).

Prevalence: ADRs are a common cause of morbidity and mortality globally. They contribute to a considerable burden on healthcare resources, resulting in increased hospitalizations, prolonged hospital stays, and additional medical expenses (Lavan, 2016).

Pharmacovigilance Systems: Many countries have established pharmacovigilance systems to monitor and report ADRs. These systems aim to collect data on suspected adverse reactions and assess the safety profiles of medications in real-world settings. The World Health Organization (WHO) collaborates with national pharmacovigilance centers worldwide to promote patient safety through the reporting and analysis of ADRs (European Medicines Agency Guideline on Good Pharmacovigilance Practices, 2012).

Reporting Mechanisms: Most countries have implemented reporting mechanisms for healthcare professionals and the general public to report suspected ADRs. These mechanisms often include national databases, online reporting platforms, or toll-free hotlines to encourage the reporting of adverse events related to medications (Kalaiselvan, 2014).

Regulatory Authorities: National regulatory authorities play a critical role in evaluating the safety of medications. They review ADR reports, conduct investigations when necessary, and may take actions such as updating drug labels, issuing safety warnings, or even removing drugs from the market to protect public health (van Grootheest, 2004).

International Collaboration: Organizations like the WHO, the Uppsala Monitoring Centre (UMC), and the International Society of Pharmacovigilance (ISoP) foster international collaboration on pharmacovigilance activities. They promote the exchange of information and best practices to enhance drug safety worldwide (Leskur, 2022).

ADR Awareness: Public awareness campaigns are conducted in many countries to educate patients and healthcare professionals about the importance of reporting ADRs. These initiatives aim to increase reporting rates and improve patient safety (Sloane, 2015).

ADRs and COVID-19 Vaccines: With the emergence of the COVID-19 pandemic, the safety of vaccines became a significant concern. Many countries have closely monitored and reported ADRs associated with COVID-19 vaccines through their respective pharmacovigilance systems (Ortiz, 2018).

National Overview: *National Pharmacovigilance Systems:* Many countries have established national pharmacovigilance systems to monitor and collect data on ADRs. These systems involve healthcare professionals, pharmaceutical companies, and regulatory authorities. The primary goal is to detect, assess, and prevent ADRs to ensure patient safety (Bahk, 2015).

Reporting Mechanisms: National pharmacovigilance systems typically have reporting mechanisms that allow healthcare professionals and the general public to report suspected ADRs. Reporting can be done through online portals, mobile applications, toll-free hotlines, or paper-based forms. These mechanisms encourage the timely and accurate reporting of adverse events associated with medications (de Vries, 2021).

National Regulatory Authorities: National regulatory authorities oversee the approval, marketing, and safety monitoring of medications within their respective countries. They play a crucial role in evaluating ADR reports and taking appropriate actions to safeguard public health. This may include updating drug labels with new safety information, issuing safety alerts or warnings, or even withdrawing medications from the market if necessary (de Vries, 2021; Pahuja, 2014).

Collaborative Efforts: National pharmacovigilance systems often collaborate with international organizations like the World Health Organization (WHO) and the Uppsala Monitoring Centre (UMC) to share information, best practices, and global safety data. Such collaborations enhance the ability to identify emerging safety concerns and contribute to a broader understanding of drug safety on an international scale (Valinciute-Jankauskiene, 2021).

Adverse Drug Reaction Databases: Many countries maintain databases that store and analyze ADR reports. These databases serve as valuable resources for healthcare professionals and regulatory authorities to monitor the safety profiles of medications used within their countries.

Public Awareness and Education: National health agencies and organizations conduct public awareness campaigns to educate both healthcare professionals and the general public about ADRs. These

initiatives aim to increase awareness about the importance of reporting suspected ADRs and promote patient safety.

ADR Monitoring and Vaccination Programs: With the administration of vaccines and other medications, national health authorities closely monitor ADRs, particularly during vaccination campaigns. Monitoring ADRs related to vaccines is crucial to ensure the safety and efficacy of immunization programs (Fortnum, 2012).

Importance of ADR reporting for drug safety

Detection of Unknown Adverse Reactions: ADR reporting allows for the identification of previously unknown or rare adverse reactions associated with medications. Early detection of such reactions can lead to prompt intervention, preventing further harm to patients (Bodenheimer, 2009).

Post-Marketing Surveillance: Clinical trials before drug approval may not capture all possible adverse reactions due to limited sample sizes and controlled conditions. ADR reporting enables continuous monitoring of drug safety in real-world settings after drugs are released to the market.

Signal Detection and Risk Assessment: Aggregating ADR reports from various sources helps in identifying patterns or signals that may indicate potential safety concerns. Analyzing these signals aids in assessing the risk-benefit profiles of drugs, leading to appropriate regulatory actions if necessary (Parameswaran Nair, 2017).

Improving Drug Labeling and Usage Guidelines: ADR reports provide valuable data that can lead to updates in drug labeling, including warnings, precautions, and contraindications. This ensures that healthcare professionals and patients are informed about potential risks and appropriate usage (Quan, 2005).

Enhancing Pharmacovigilance Practices: ADR reporting contributes to the overall improvement of pharmacovigilance systems and practices. Regular analysis of ADR data can lead to enhancements in reporting processes and signal detection methodologies.

Understanding Drug Interactions and Comorbidities: ADR reporting helps in assessing the interactions between multiple medications and the influence of underlying medical conditions, providing valuable insights for personalized medicine and treatment plans (Gould, 2015).

Patient Empowerment: Encouraging patients to report ADRs empowers them to actively participate in their healthcare. Patient-driven ADR reporting can lead to improved patient safety and better healthcare outcomes (Zhang, 2019).

Post-Approval Safety Assessment: ADR reporting assists regulatory agencies in ongoing evaluations of drug safety profiles. It helps in reevaluating the risk-benefit balance of drugs to ensure continued safety and efficacy.

Challenges in ADR Reporting

ADR reporting faces several challenges that impact its effectiveness and completeness. Some of the key challenges include:

Underreporting: One of the most significant challenges is the underreporting of adverse drug reactions. Healthcare professionals and patients may not always recognize or report ADRs, leading to a significant gap in the data collected. Underreporting can hinder the detection of rare or long-term adverse reactions, potentially delaying necessary interventions.

Reporting Bias: ADR reporting is susceptible to reporting bias, where certain adverse reactions may be overreported or underreported due to various factors such as media attention, public perception, or the drug's popularity. This bias can distort the true safety profile of a medication (Zhang, 2009).

Lack of Awareness: Healthcare professionals and patients may have limited awareness and understanding of the importance of ADR reporting. Lack of knowledge about reporting mechanisms, uncertainty about causality, or fear of repercussions can deter reporting (Rottenkolber, 1992).

Time Constraints and Workload: Healthcare professionals often face time constraints and heavy workloads, which can discourage them from dedicating time to reporting ADRs. Reporting processes may be perceived as time-consuming and cumbersome, reducing participation rates (Schumock, 1992).

Difficulty in Causality Assessment: Determining the causality between a drug and an adverse reaction can be challenging, especially when patients are taking multiple medications or have underlying health conditions. Establishing a clear cause-and-effect relationship is essential for accurate reporting (Shepherd, 2012).

Incomplete or Inaccurate Information: ADR reports may lack crucial details, such as patient demographics, drug dosage, and concomitant medications, making it difficult to assess the seriousness and validity of the reported adverse reaction (Scondotto, 2018).

Patient Involvement: Patient reporting of ADRs is gaining recognition, but challenges remain, including patient awareness, the ability to differentiate ADRs from other symptoms, and limited access to reporting channels (Oscanoa, 2017).

Incentives for Reporting: There may be a lack of proper incentives for healthcare professionals and patients to report ADRs. Encouraging and rewarding ADR reporting efforts could enhance participation rates.

Data Quality and Signal Detection: Large volumes of ADR reports can pose challenges in signal detection and analysis. Ensuring data quality and implementing effective data mining techniques are essential to identify relevant safety signals (Obreli-Neto, 2012b).

Resource Constraints: Some healthcare settings, especially in low- and middle-income countries, may lack sufficient resources and infrastructure to support robust pharmacovigilance and ADR reporting systems (Mateti, 2011 and Montastruc, 2018).

Propose strategies for enhancing ADR reporting and pharmacovigilance in the future

Enhancing ADR reporting and pharmacovigilance in the future requires a comprehensive and collaborative approach involving various stakeholders. Here are some strategies to consider:

- Launch targeted awareness campaigns to educate healthcare professionals, patients, and the general public about the importance of ADR reporting. Highlight the role of pharmacovigilance in ensuring drug safety and its impact on patient care.
- Streamline ADR reporting systems and make them user-friendly for healthcare professionals and patients. Implement digital platforms and mobile applications that facilitate easy and efficient reporting, reducing the burden on reporters.
- Establish incentives for healthcare professionals and patients to report ADRs, such as acknowledgment, Continuing Medical Education (CME) credits, or other rewards. Recognizing their contributions can boost reporting rates.
- Empower patients to actively participate in their healthcare by encouraging patient-driven ADR reporting. Provide clear instructions on how patients can report ADRs and assure them that their contributions are valued.
- Promote collaboration between healthcare institutions, regulatory agencies, and pharmaceutical companies for effective data sharing and signal detection. Share de-identified ADR data to improve the overall safety assessment.
- Leverage advanced technologies, such as natural language processing and machine learning algorithms, to automate ADR

signal detection and improve data analysis. AI-based systems can identify potential safety signals more efficiently.

- Integrate real-world data from electronic health records, patient registries, and social media platforms into pharmacovigilance efforts. This data can enhance the understanding of drug safety in diverse patient populations.
- Implement data validation processes and quality checks to ensure accurate and complete ADR reporting. Standardize reporting forms and terminology to improve data consistency.
- Encourage international collaboration and information exchange among pharmacovigilance programs. Collaborative efforts can improve the detection of global safety signals and enhance drug safety assessments.
- Establish regular evaluations of pharmacovigilance systems to identify areas for improvement. Use feedback from healthcare professionals and patients to refine reporting processes and address challenges.
- Regulatory agencies should play an active role in promoting ADR reporting and providing clear guidelines for reporting requirements. Timely feedback on reported ADRs can foster a culture of safety and accountability.
- Support research on ADR reporting and pharmacovigilance to explore innovative methods for signal detection, improve causality assessment, and assess the impact of reporting interventions (Linskey and McLeod, 2021).

Mobile application to enhance ADR reporting and pharmacovigilance: Developing a mobile application to enhance ADR reporting and pharmacovigilance can be an effective and user-friendly approach. Here are some strategies for designing and implementing such an application that will have a user-friendly interface. Design an intuitive and user-friendly interface that simplifies the ADR reporting process (Avong, 2018). The app should be easy to navigate, with clear instructions and minimal data entry requirements.Ensure the mobile app is available on multiple platforms (iOS, Android, etc.) to reach a wider audience of healthcare professionals, patients, and consumers (Herdeiro, 2012). The implementation of push notifications to remind users to report ADRs and provide updates on the status of their reports. Also, regular reminders will encourage consistent reporting. The app can show multilingual Support and offer to accommodate users from different regions and language preferences, making it accessible to a broader global audience (Baron, 2013).

CONCLUSION

In conclusion, this narrative review emphasizes the indispensable role of ADR reporting in pharmacovigilance and drug safety. By identifying and addressing current challenges, healthcare systems can take significant strides toward a more robust and patient-centric approach to ADR monitoring. The integration of advanced technologies and collaboration among stakeholders is essential to advance the field of pharmacovigilance and enhance patient outcomes through timely and accurate ADR reporting.

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