



Artificial Intelligence in Pharmacovigilance: A future to Manage Adverse Drug Reactions

Pramod Kumar Manjhi^{1*}, Vikas Maharshi²

¹Professor (Assoc.) & Head, Department of Pharmacology, ²Professor (Assoc.), Department of Pharmacology, All India Institute of Medical Sciences, Patna – 801507 (Bihar) India.

Phocomelia was reported in Germany during (1961-62) when thalidomide was prescribed for the treatment of morning sickness. This is the greatest of all drug disasters that opened the World's eyes to the safety of drugs. Pharmacovigilance (PV) has been derived from the Greek word *Pharmakon*, which means a drug, and the Latin word *Vigilare*, meaning observant.¹ In simple words, PV is to keep watch on the use of drugs. In 2002, the World Health Organisation defined PV as the 'science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problems.'

Adverse Drug Reactions (ADRs) have been defined as 'any noxious change which is due to a drug, occurs at doses normally used in man, requires treatment or decrease in dose or indicates caution in the future use of the same drug'. Since ADRs continue to occur even after a new drug is released for use in the community, careful PV must continue to avoid such tragedies that occurred following thalidomide use.

The Pharmacovigilance Programme of India (PvPI) was launched in July 2010, by the Central Drugs Standard Control Organisation (CDSCO) under the Director General of Health Services, the Ministry of Health & Family Welfare, Government of India to monitor the ADRs to enhance patient safety. The Indian Pharmacopoeia Commission works as the National Coordination Centre (NCC) which is supported by ADR Monitoring Centres across the country. The mission of the programme is to ensure that the benefits of the use of medicine outweigh the risks and thus safeguard the health of the Indian population.

AI may be useful in PV for the automatic execution of tasks associated with case report processing; The identification of clusters of adverse events (AE) representing symptoms of syndromes; The objectives of PvPI are to monitor ADRs in the Indian population; to create awareness amongst HCPs about the importance of ADR reporting in India; to monitor

the benefit-risk profile of medicines approved, marketed and used in the country; to generate independent evidence-based recommendations on the safety of medicines; to communicate safety-related findings to all stakeholders; to support the CDSCO in formulating safety-related regulatory decisions for medicines; to create a national centre of excellence at par with global drug safety monitoring standards.

ARTIFICIAL INTELLIGENCE IN PHARMACOVIGILANCE

According to the Father of Artificial Intelligence (AI) John Mc Carthy, it is, "The science and engineering of making intelligent machines". Artificial Intelligence refers to the ability of a computer or a computer-enabled robotics system to process information and produce outcomes like the thought process of humans in learning, decision making and solving problems.² The AI system aims to develop a system capable of solving complex problems in ways similar to human logic and reasoning.³

Conduction of pharmacoepidemiological studies, and the prediction and prevention of AEs through specific models using real-world data; the technical challenges for AI-based PV are a lack of high-quality databases, insufficient human resources, weak AI technology and insufficient support from governments.

AI TOOLS AND METHODS USED IN PV:⁴

- **VigiBase:** WHO global database of individual case safety reports. The global repository of reported adverse effects of medicines for human use including herbals, biologicals and vaccines. The data is structured by WHO Drug and MedDRA and continuously updated with reports shared by member countries of

Corresponding Author:

Pramod Kumar Manjhi, Professor (Assoc.) & Head, Department of Pharmacology, Department of Pharmacology, All India Institute of Medical Sciences, Patna – 801507 (Bihar) India; Email: drpramodkumar@aiimspatna.org

ISSN: 2231-2196 (Print)

ISSN: 0975-5241 (Online)

Received: 08.11.2023

Revised: 30.11.2023

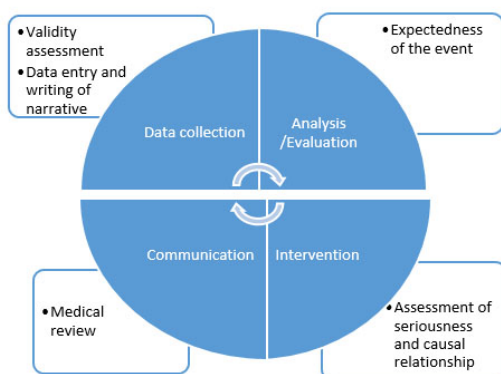
Accepted: 13.12.2023

Published: 30.12.2023

the WHO Programme for International Drug Monitoring to allow for timely identification of potential safety concerns

- **VigiAccess:** It is a publicly accessible web application to browse and easily access adverse drug effects' data easily through VigiBase.
- **VigiLyze:** Online resource that provides a quick and clear overview of VigiBase. It allows exploration of VigiBase through instant demographic overviews, case series, line listings, case details and disproportionality measures that can be further explored online or exported for further analysis. Structured data allows for easy aggregation and quick and easy drill down by e.g reaction, age group and country. VigiLyze is available to member countries of the WHO Programme for International Drug Monitoring.
- **VigiFlow:** A web-based individual case safety report management system. Supports the national collection, processing and sharing of reports with relevant stakeholders. Data is structured with WHO Drug and MedDRA codes to facilitate effective analysis. It is available to member countries of the WHO Programme for International Drug Monitoring but not a mandatory requirement for reporting to VigiBase. An Internet connection is required, as no offline functionality is available.
- **VigiGrade:** A measure of report quality. It provides a completeness score for the amount of clinically relevant information available in a structured format on individual case safety reports. This is mainly used as a part of communication with countries on data quality.
- **VigiMatch:** An algorithm for automated duplicate detection. It detects suspiciously similar pairs of individual case safety reports, using probabilistic pattern matching.
- **VigiRank:** A statistical signal detection method for pharmacovigilance. Uses a predictive model to rank potential safety signals in VigiBase based on overall reporting patterns and the quality and content of individual reports.

DATA FLOW AND SCOPE OF AI IN PV:



How ADR can be managed by AI?

AI and Machine Learning models are being applied to improve the PV process, including case intake using Optical Character Recognition and Natural Language Processing, natural language generation for narrative writing, robotic process automation for dynamic case workflow, AI-based signal detection, and AI-based adverse event prediction. These advancements have the potential to increase efficiency, accuracy, and consistency in PV, as well as reduce costs and delivery timelines for regulatory decisions.

Benefits of AI in ADRs Reporting System/PV:

The most important benefit of AI is reduced cycle times. Due to this method, the processing is spontaneous. It can be used for the identification of ADRs. AI can handle or manage diverse types of incoming data formats. AI is useful to reduce the burden and time of case processing. Improve the quality and accuracy of the information. AI tools extract the information from the adverse drug event form and evaluate the case validity without the workforce. AI has an economic impact on reducing the cost of ADR reporting processes.

The advantage of an AI-based PV system includes-Automatic detection, an evidence generation network, Multiple data source integration, AI algorithms optimization, and Concept standardization. This could largely help minimize the human labour workload and facilitate the development of PV.

Challenges with AI in PV:

There are some challenges with using AI in PV which include:

- **Data Quality and Availability:** The quality and quantity of data can affect the performance of AI models. In PV, data may be incomplete, inconsistent, or biased, which can lead to inaccurate or unreliable results.
- **Explainability:** AI can be difficult to interpret and explain, which can be a problem in a regulated field such as PV where decisions may have significant consequences.
- **Legal and Ethical Considerations:** AI in PV may raise legal and ethical concerns, such as inadvertent bias and liability concerns.
- **Integration with existing systems:** AI may need to be integrated with existing systems and processes, which can be a challenging task.
- **Validation and Regulatory Approval:** AI in PV may need to be validated and approved by regulatory bodies before they can be used in practice.

CONCLUSION

Artificial intelligence allows for the processing and analysis of large amounts of data and can be applied to various disease states.⁵ The automation and machine learning models

can optimize PV processes and provide a more efficient way to analyze information relevant to safety, although more research is needed to identify if this optimization has an impact on the quality of safety analyses. It is expected that its use will increase soon, particularly with its role in the prediction of side effects and ADRs. At present, awareness about AI in PV is in its infancy.

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