**Artificial intelligence in pharmacovigilance**

 Shubhangi Dukare, Priti Pokharkar , Aditi Pawar, Vinit Bankar. Ganesh Lamkhade

 Department of Pharmaceutics

 Samarth Institute of Pharmacy ,Belhe.Pune412410,Maharashtra,India

**Abstract**

Automation has the potential to revolutionize pharmacovigilance by reducing case reporting costs and improving data quality to truly provide value, including drug safety signal detection. Pharmacovigilance through analytical and benefit-risk analysis. Technological developments have a big impact on how pharmaceutical PV strategies evolve. For instance, more companies are realizing how important big data analytics, cloud-based solutions, mobile apps, robotic automation, and artificial intelligence are to the clinical safety and regulatory procedures of the pharmaceutical industry. Implementing state-of-the-art technological automation tools and procedures for PV approaches is becoming more and more crucial for managing the safety of pharmaceutical items. Pharmacovigilance's ability to identify, monitor, manage, and report adverse drug reactions (ADRs) more efficiently can be enhanced using artificial intelligence and machine learning. The primary goal of artificial intelligence is to solve problems that cannot be solved automatically, such as obtaining the right training data for machine learning models and the requirement for unified regulatory guidelines. Fast-moving AI that never gets tired or ill can analyze and comprehend data at breakneck speeds. The ICSR in PV, which includes native automation and standalone technologies like AI and ML that decrease manual labor, processes thousands of adverse impacts each month.

**Keywords** – Automation, Health care system, Automation in Pharmacovigilance, Machine Learning [ML], Artificial Learning [AI].

**Introduction**

Pharmacovigilance: The Etymological roots for the word “Pharmacovigilance” are Pharmakon (Greek) = medicinal substance, and Vigilance (Latin) = to keep watch.(1)

Pharmacovigilance (PV), as defined by the WHO, is the science and practice of identifying, evaluating, comprehending, and preventing side effects or other drug-related issues. Across the globe, adverse drug reactions are reported in a multitude of languages and formats, as well as in handwritten, unwritten, and organized paperwork; on average, multiple firms receive over 3 lakh ADRs every year. Human error is possible with manual operations, which ultimately raises the project's overall cost. AI-based technology can be used to facilitate the evaluation and extraction of case validity from AE source documents. Automation is the process of using technology to perform or remove jobs to reduce reliance on humans. Numerous government health officials engage in pharmacovigilance initiatives on either a daily or irregular basis. According to Lewis and McCallum, artificial intelligence (AI) and machine learning (ML) have started to change how safety and pharmacovigilance (PV) professionals handle and analyze data to aid in decision-making.[1, 2, 3]

The study of adverse event assessment, prevention, detection and collection, and evaluation of drug-related issues is known as pharmacovigilance. Although the number of individual case safety reports may rise annually, 90% of adverse occurrences (AEs) remain unreported. Therefore, technology must be required to sustain negative events. Artificial intelligence facilitates decision-making in challenging circumstances. To evaluate PV users for decision-making, cognitive services are being created. Therefore, the strategy to overcome AEs' unreported data is to apply AI. Using social media to spread awareness of health information is another tactic. Patient narrative data is represented by electronic health records or EHRs. AEs can identify and get better by using the sources mentioned above. AI can decrease manual labor in transcribing and data input while increasing attention to the scientific and medical evaluation of adverse events, which is better for patient health (10). Artificial Intelligence (AI) is the ability of a digital machine to accomplish tasks that need human intelligence. Artificial Intelligence (AI) refers to the application of learning technologies to machines via the utilization of historical data to address future issues. AI improves clinical trial success rates and aids with patient randomization. The three biggest global health burdens are diabetes, cancer, and diabetic retinopathy. AI has demonstrated promising outcomes in the identification, prevention, treatment, and mitigation of these conditions. To guarantee the safety of continuing medical goods, PV data is crucial. It is anticipated that quality reporting and increased accuracy will result from the AI's implementation of PV data. In 1995, Netwell and Simon discovered the first AI program. The Father of AI is John McCarthy. In 1943, Warren McCulloch and Walter Pits proposed the artificial neuron model and Donald Hebb modified the strength of the connection between neurons. Because it necessitates the gathering, processing, and analysis of vast amounts of data obtained from several, divergent sources, pharmacovigilance (PV) is essentially a data-driven field [4]. Individual case safety reports (ICSRs), which are records of suspected adverse occurrences gathered through various routes, combined and arranged into sizable databases, and continuously analyzed to identify safety signals, are the main kind of data utilized in PV [5]. Chatbot interactions, electronic health records (EHRs), published literature, patient registries, patient support programs, and even direct patient communications via social media are some of the many sources of ICSRs [6]. Reports are gathered all around the world and are distinguished by differences in language, format, and the distinctive features of the underlying healthcare systems. To detect possible new safety concerns with medications and vaccinations, adverse events need to be found and examined.

The role of healthcare practitioners is evolving as a result of artificial intelligence's incorporation into the healthcare system, which also presents new opportunities to enhance patient safety outcomes [7] and care quality [8]. In both inpatient and outpatient settings, artificial intelligence is being applied to enhance patient safety [9]. By using digital strategies that facilitate communication between patients and their healthcare providers, it has also been used to reduce avoidable harm [9]. Artificial intelligence is being used more and more in pharmacovigilance in several areas, such as target population identification, signal management, and safety operations. It is necessary to comprehend the state of artificial intelligence in pharmacovigilance today and the prospects for future development in this field.

**Artificial Intelligence**

AI research is defined by computer science as the theory and creation of computer systems that can carry out activities that often require human intelligence, such as speech recognition, visual perception, decision-making, and language translation. The study of "intelligent agents"—that is, any gadget that senses its surroundings and acts to increase the likelihood that it will accomplish its objectives—is another aspect of artificial intelligence (AI) (Poole et al, 1998; Russell and Norvig, 2003; Nilsson, 1998; Legg and Hutter, 2007).

AI, sometimes known as "computational intelligence," is widely utilized in domains including self-driving cars, robots, and gaming. As said earlier, we can presume that most existing PV applications fall closer to the ML area because AI entails the ideas of decisions and actions.

Computer science includes artificial intelligence. An artificial intelligence (AI) system utilizes an algorithm and a database of facts to create robots that mimic human behavior that,twhicholves comprehension, creative writing, speech recognition, and decision-making.[12] Similar to how a toddler learns from instruction and training in its surroundings to become an intelligent human being, the machine gains human intelligence through learning and training on a vast number of reliable datasets. To educate computers to process information similarly to the human brain and solve problems that call for human comprehension and reasoning, the new technology uses deep learning and natural language processing techniques using neural networks, which are similar to the neurons in the human brain.[13]

**Need for artificial intelligence.**

PV was created and put into use to improve patient safety for those who are exposed to diverse medications for extended periods during clinical studies. These patients include pregnant women, members of racial groups, the elderly population, and children. [13] Using a fast-track approach, PV conducts risk assessment and communication regarding the efficacy of a variety of life-saving medications, including antitubercular, antiviral, and anticancer medications. PV is still a very new field of study with little significance in many nations. Countries all around the world are voicing concerns about the necessity of mechanisms to keep an eye on the safety of medications after they are marketed.[15] The two major ways that adverse drug reactions (ADRs) are reported are spontaneously or by pharmaco-epidemiological techniques that employ methodical data collecting and analysis of adverse events (AE) associated with the use of drugs. Adverse Drug Reaction Monitoring Centers and marketing authorization holder (MAH) companies also do this to address new issues, document warning signs, and communicate to reduce or avoid harm. PV's most difficult tasksinclude technical AE coding, ADR detection and reporting, seriousness assessment, safety individual report preparation, and interaction with suspicious drugs. All of these processes, particularly ADR reporting, take a lot of time and require new and improved technology. To make it easier to maintain and process quality and compliance standards, the pharmaceutical sector and professional services collaborated to find a new technology called artificial intelligence that makes it simple to track globally accessible data, something that other available methods. AI methods are important in the fields of medication development and pharmaceutical product adverse event detection.[14]

**ROLE OF AI IN PV IN 21st CENTURY**

According to real-world data, PV has to develop specific plans because AI is at least partially the answer for cancer and many other severe and fatal illnesses. Since AI is a source that generates electronically useful healthcare information, patient-level information from individual consumers is not always the same as validated data in the realm of big data outcomes. PV operations are essential for modernizing the post-marketing surveillance of biosimilars in the twenty-first century. The initial strategy for AI in PV is to create a new epidemiological concept based on an awareness of the distinction between "generic" and "biosimilar." According to Herbert Simon, "design thinking" in the artificial sciences is the "transformation of existing conditions into preferred ones." The analysis of ideas that are action-oriented and created by AI is known as critical thinking. "The fear is not that we will discover new information, but that we will become overwhelmed with our current capacity of poor-quality information," Dr. Donald Therese stated at a recent conference. (17)

**Applications of AI in PV**

1. **Regulatory**

Although AI has been developed and applied in a number of PV domains, it is not yet sufficiently developed for widespread application. With new drugs being expedited via the FDA's new regulatory channels, the COVID-19 pandemic illustrated the value of a quick, flexible strategy. The FDA published a five-year roadmap for incorporating AI into the pre-existing PV framework even before the epidemic.(18)

1. **Clinical**

It takes roughly 10–12 years, including 5–6 years of clinical trials, for a medicine to be approved and put on the market. Certain procedures, such patient recruiting and site selection, take a lot of time during clinical trials and frequently result in trial failure for a variety of reasons. Pharmaceutical businesses are therefore anticipating new technologies such as artificial intelligence (AI) to lower the cost of research and development, analyze a huge number of instances, and help personalize data (19).

**Forms of AI**

**1.Machine Learning**

AI allows the software to learn and study the machine over a time without following the explicit instructions and improves from previous data to enhance its behavior and create new predictions.(20)

**2.Supervised Learning**

In these algorithms are used to predict appropriately which label corresponds to an individual component. Thus, the input of AI is labelled with the corresponding output. (21)

**3.Unsupervised Learning**

It is basically machine learning type in which algorithms are used to analyse the unlabeled data 17 Although the model is using unlabeled data, it looks for recurring patterns that exist within the input data.[22]

**4.Semi-supervised Learning**

It is the combination of unsupervised and supervised learning. Here, labeled data are combined with unlabeled data to earn the predict models better. Semi-supervised learning algorithms are used when the data is incomplete.[22]

**5.Reinforcement Learning**

It is used when prior experiences are used to make adequate decisions. The prior experience helps in improving the algorithms with the help of constant feedbacks. 16 AE can be prevented by focusing on specific traits.[22]



**Current role of AI in healthcare**

Continuous learning of repeated data-rich tasks with a clear indication of a good outcome is where artificial intelligence and machine learning have the biggest influence. IBM and colleagues were able to differentiate between normal and subpar screening tests and predict biopsy-proven malignancy using health data and a retrospective machine-learning analysis of mammography images. The researchers claim that their algorithm may assess breast cancer at a level "equivalent to radiologists" and might greatly lower the number of breast cancer diagnoses that are missed.[23] Another example of the use of AI in healthcare is the prediction of asthma attacks, mobile applications for insulin monitoring, osteoporosis risk group identification, tracking the effectiveness of anticoagulant medication compliance, and TB [tuberculosis] control.

Additionally, by decoding brain activity, recurrent neural networks generate voice acoustics, and machine learning is used to more effectively identify and potentially enroll participants in prospective studies, such as randomized clinical trials. Collectively, these examples demonstrate the breadth of advancements in healthcare that AI/ML has enabled. New understandings of illness and its progression, as well as the provision of healthcare, are made feasible by safety, which has the same general criteria and potential opportunities.[24]

Importance of AI and Automation in pharmacovigilance

Pharmacovigilance processes can benefit from the application of AI and automation in signal detection, monitoring, risk management, adverse event intake, and report generation.[26, 30]

Automated case processing and signal identification: At several points during the process, automation can help with case processing. An automated system can understand both structured and unstructured data from a range of sources by using natural language processing, or NLP. The processes in the process include identifying duplicates, examining data to find phrases or patterns that indicate significant patient risks or unknown adverse events, and reporting data following evaluation.[27]

Post-marketing surveillance (PMS), or tracking the safety of medications after a product has been put on the market, is an area where AI and automation can greatly improve. Mostly due to the vast amount of real-world data that can now be merged, including case reports, academic literature, and ongoing monitoring.[28, 29]

**Advantages**

1. **Machine learning[ML]**-

Unsupervised learning has no ground truth and is utilized for signal management, but supervised learning used in PV for ICSR processing may train ML algorithms where ground truth, i.e., Human annotated response file.[31]

1. **Semantic search** –

 improve the comprehension of searchers.

1. **Optical character recognition (OCR)** –

detect text in scanned documents, as well as for handwritten Text verification.

1. **Chabot’s –**

NLP may be used to perform human conservation using text or voice methods.

**5.Text analysis** –

 investigate gathered data from sources into evidence by structuring unstructured text.

**6.Sentiment analysis** –

 in the sense of text extraction from context[32,33]

**7.Increased Speed** :

 AI can process large amounts of data much faster than traditional methods.

**8. Improved Accuracy** : AI can reduce the risk of human error, improving the accuracy of data analysis and insights.

**9. Scalability** :

AI can handle large amounts of data, making it an ideal solution for pharmaceutical companies with large datasets.

**10. Cost Savings** :

 AI can automate manual processes, reducing the time and cost associated with data analysis and insights.

**11. Competitive Advantage:**

 Pharmaceutical companies that leverage AI can gain a competitive advantage in the market, improving their ability to bring new treatments to market quickly and efficiently.

**Technical Challenges**

**1. Data Quality and Standardization**\_: Ensuring high-quality and standardized data for AI model training and validation.

**2. Algorithmic Bias and Fairness\_:** Mitigating bias in AI models to ensure fairness and accuracy in safety signal detection.

**3. Explainability and Transparency**\_: Developing explainable and transparent AI models to facilitate understanding of safety signal detection.

**4. Scalability and Integration**\_: Scaling AI solutions to accommodate large datasets.

One of the most important and vital roles in healthcare is pharmacovigilance. The application of artificial intelligence (AI) in this domain is still in its infancy, though. The availability of organized and curated data to train the software to detect possible medication safety hazards is one of the primary obstacles to AI adoption. Furthermore, utilizing AI for pharmacovigilance raises privacy issues because data may be utilized for other purposes without the participants' consent (19).combining them with the pharmacovigilance systems that are currently in place.

**CONCLUSION**

AI in health care has been very impressive for a well-defined, discrete task like the interpretation of medical images; however, its application to heterogeneous data is complicated. The application of AI tool to PV system has potential benefits to minimize the burden of manual workload and boost efficiency. However, it cannot replace or overtake the importance of medical review and judgment of trained PV professionals for final adjudication of causality and signal detection. To date, full automation of PV system comes at risks and several challenges. It requires more testing, validation, and approval from medical professionals and regulators. Neither AI experts appreciate the intricacy and complexity of the interpretation of medical data nor do medical professionals comprehend the operations of AI technology. AI technology should enhance human intelligence rather than substitute human experts. What is important is to emphasize and ensure that AI brings more benefits to PV rather than challenges.

**Referance**

1. Divya, P., Susmita, A., Sushmitha, P., Ch, R. and Chandini, K., 2022. Automation in pharmacovigilance: artificial intelligence and machine learning for patient safety. Journal of Innovations in Applied Pharmaceutical Science (JIAPS), pp.118-122.

2. Bate, A. and Hobbiger, S.F., 2021. Artificial intelligence, real-world automation and the safety of medicines. Drug Safety, 44, pp.125-132.

3. Rifat, M.J.R., Noori, S.R.H. and Hasan, M.R., 2019, July. Pharmacovigilance study of opioid drugs on Twitter and PubMed using artificial intelligence. In 2019 10th International Conference on Computing, Communication and Networking Technologies (ICCCNT) (pp. 1-7). IEEE.

4. Mann RD, Andrews EB. Pharmacovigilance. John Wiley & Sons;2007.

5. Office of the Commissioner. Individual Case Safety. 2019. Available at: https://www.fda.gov/industry/fda-resources-datastandards/individual-case-safety-reports

6. Stergiopoulos S, Fehrle M, Caubel P, Tan L, Jebson L. Adverse drug reaction case safety practices in large biopharmaceutical organizations from 2007 to 2017: an industry survey. Pharmaceutical Med. 2019;33(6):499–510.

7. Macrae C. Governing the safety of artificial intelligence in healthcare. BMJ Qual Saf. 2019;28(6):495– 8.

8. Grossman LV, Choi SW, Collins S, Dykes PC, O’Leary KJ, Rizer M, et al. Implementation of acute care patient portals: recommendations on utility and use from six early adopters. J Am Med Inf Assoc. 2018;25(4):370–9.

9. Bates DW, Levine D, Syrowatka A, Kuznetsova M, Craig KJT, Rui A, et al. The potential of artificial intelligence to improve patient safety: a scoping review. NPJ Digit Med. 2021;4(1):54

10. Mockute R, Desai S, Perera S, Assuncao B, Danysz K, Tetarenko N, et al. Artificial Intelligence Within Pharmacovigilance: A Means to Identify Cognitive Services and the Framework for Their Validation. Pharmaceut Med [Internet]. 2019;33(2):109–20. Available from: https://doi.org/10.1007/s40290-019-00269-0

11. Russel and Norvig, 2003; Nilsson, 1998; Legg and Hutter, 2007).

12. Aronson JK. Artificial intelligence in pharmacovigilance: An introduction to terms, concepts, applications, and limitations. Drug Saf 2022;45:407-18.

13. Ibrahim H, Abdo A, El Kerdawy AM, Eldin AS. Signal detection in pharmacovigilance: A review of informatics-driven approaches for the discovery of drug-drug interaction signals in different data sources. Artif Intell Life Sci 2021;1:100005

14. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6984023/#ref19 Venulet J, Helling-Borda M. WHO's international drug monitoring – The formative years, 1968-1975: Preparatory, pilot and early operational phases. Drug Saf. 2010;33:e1–23. [PubMed] [Google Scholar] [Ref list]

15. Report of CIOMS Working Group IV. Geneva: CIOMS; 1998. Council for International Organisations of

16. Medical Sciences. Benefitrisk balance for Marketed drugs: evaluating safety signals. No. 762. [Google Scholar] [Ref list]

17. Pitts PJ. 21st Century Pharmacovigilance: Intuition, Science, and the Role of Artificial Intelligence. J Commer Biotechnol. 2017;23(1):3–6

18. Basile AO, Yahi A, Tatonetti NP. Artificial intelligence for drug toxicity and safety. Trends Pharmacol

Sci. 2019;40:624–35. [PMC free article] [PubMed] [Google Scholar] [Ref list]

19. Ball R and Dal Pan G. “Artificial intelligence” for pharmacovigilance: ready for prime time?. Drug

Saf. 2022;45: 429–438. https://doi.org/10.1007/s40264-022-01157-4.

20. Mcgrail S. AI in the pharma industry: current uses, best cases, digital future. Pharmanews Intelligence. 2021 April. Accessed 21 August 2022. https://pharmanewsintel.com/news/ai-in-the-pharma-industry-currentuses-best-cases digitalfuture#:~:text=AI%20has%20a%20great%20potential,during%20the%20COVID%2D19%20pandemic.

21. Holzinger A, Langs G, Denk H, et al. Causability and explainability of artificial intelligence in medicine. 2019 April. Accessed 18 August 2022. doi: https://doi.org/10.1002/widm.1312

22. Rossello J. Machine learning and pharmacovigilance. Pharmacovigilance analytics. 2022 March. Accessed

23. August 2022. https://www.pharmacovigilanceanalytics.com/methods/artificial intelligence/machinelearning-and-pharmacovigilance/.

24. Gupta R, Srivastava D, Sahu M, et al. Artificial intelligence to deep learning: machine intelligence approach for drug discovery. Mol Divers. 2021;25(3):1315-1360. doi:10.1007/s11030-021-10217-3.

25. IBM Cloud Education. Unsupervised learning. 2020 September. Accessed 18 August2022. https://www.ibm.com/cloud/learn/unsupervised-learning

26. Babu, A., Sabu, S.T. and Dharan, S.S., 2020. ARTIFICIAL INTELLIGENCE: AN INNOVATIVE

APPROACH IN PHARMACOVIGILANCE.

27. Lewis, D.J. and McCallum, J.F., 2020. Utilizing advanced technologies to augment pharmacovigilance

systems: challenges and opportunities. Therapeutic innovation & regulatory science, 54, pp.888-899.

28. Danysz, K., Cicirello, S., Mingle, E., Assuncao, B., Tetarenko, N., Mockute, R., Abatemarco, D., Widdowson, M. and Desai, S., 2019. Artificial intelligence and the future of the drug safety professional. Drug safety, 42, pp.491-497.

29. Wani, P., Shelke, A., Marwadi, M., Somase, V., Borade, P., Pansare, K. and Sonawane, G., 2022. ROLE OF Artificial INTELLIGENCE IN PHARMACOVIGILANCE: A CONCISE REVIEW. Journal ofPharmaceutical Negative Results, pp.6149-6156.

30. Kompa, B., Hakim, J.B., Palepu, A., Kompa, K.G., Smith, M., Bain, P.A., Woloszynek, S., Painter, J.L.,Bate, A. and Beam, A.L., 2022. Artificial intelligence based on machine learning in pharmacovigilance: ascoping review. Drug Safety, 45(5), pp.477-491.

31. Mockute, R., Desai, S., Perera, S., Assuncao, B., Danysz, K., Tetarenko, N., Gaddam, D., Abatemarco, D., Widdowson, M., Beauchamp, S. and Cicirello, S., 2019. Artificial intelligence within pharmacovigilance: a means to identify cognitive services and the framework for their validation. Pharmaceutical medicine, 33, pp.109-120.

32. Salas, M., Petracek, J., Yalamanchili, P., Aimer, O., Kasthuril, D., Dhingra, S., Junaid, T. and Bostic, T.,2022. The Use of Artificial Intelligence in Pharmacovigilance: A Systematic Review of the Literature. Pharmaceutical medicine, 36(5), pp.295-306

33. Ball, R. and Dal Pan, G., 2022. “Artificial Intelligence” for Pharmacovigilance: Ready for Prime Time?. Drug Safety, 45(5), pp.429-438.

34. Hauben M, Hartford CG. Artificial Intelligence in Pharmacovigilance: Scoping Points to Consider. Clin Ther [Internet]. 2021;43(2):372–9. Available from: https://doi.org/10.1016/j.clinthera.2020.12.014.

35. S alas, M., Petracek, J., Yalamanchili, P., Aimer, O., Kasthuril, D., Dhingra, S., Junaid, T., & Bostic, T. (2022). The Use of Artificial Intelligence in Pharmacovigilance: A Systematic Review of the Literature. Pharmaceutical medicine, 36(5), 295–306. https://doi.org/10.1007/s40290-022-00441-z.