Role of AI in Pharmacovigilance and Drug Safety: A Review

Tanu Priya, Prof (Dr) Kapil Kalra, Tanya Raj, Pragyanjali Lahon, Arpit Kumar, Deepak Rawat
Alpine College of Management and Technology, Dehradun

***Abstract*- In 1961. the World Health Organization (WHO) has established the Pharmacovigilance (PV) program in response to the thalidomide disaster, for global drug monitoring. PV is the science and activity relating to the detection, assessment, understanding and prevention of adverse effect and any other drug related problems. The aim of PV is to improve patients care and safety in relation to the use of medicine and all medical and paramedical interventions. The program has broadened its concerns by including herbals, traditional and complementary medicines, blood products, medical devices, herbal vigilance, hemovigilance and materiovigilance. Drug safety is mitigation exercise in which ADRs caused by therapeutics drug biologicals or devices can be explore, prevent or minimized. PV is collecting a huge amount of data daily and it is a challenging task to process these vast collected data. Al holds potential to transform Pharmacovigilance and is effective to improve PV activities. Examples of Al applications in Pharmacovigilance include the use of disproportionality analysis to regulate drug event combinations with subsequent expansions to drug-drug interactions and risk factors, syndrome detection, predictive models for statistical signal detection and case triaging. Al aim to achieve efficiency, quality and capability of drug in Pharmacovigilance.**

***Keywords*- Pharmacovigilance, thalidomide, AI, detection, adverse effect**

I. INTRODUCTION

The word “Pharmacovigilance” was derived from the Greek literature “Pharmakon” means drug and the word “vigilare” means to keep watch in Latin. The Pharmacovigilance program was established by the World Health Organization (WHO) in 1961 in response to the thalidomide tragedy, for worldwide drug surveillance. PV is the field of study and practice concerned with the detection, evaluation, comprehension and avoidance of adverse drug effects or any other potential drug-related issues.[1]

The Drug Safety Professional
Numerous DS team members participate in a range of procedures from ICSR reception to submission to regulatory bodies. This calls for specialized expertise and competencies [2]. The DS/pharmacovigilance core competency was proposed by King [3]. characteristics outlining the DS scientific knowledge required for You work as a professional in DS. Extra Among the fundamental capabilities are analytical and evaluation abilities, Proficiency in communication, leadership, and systems thinking abilities. An entry-level position requires Level 1: core competencies.
Level 2: key competencies are applicable to level DS professionals. Senior and advanced DS colleagues, managers
Level 3: core competences are applicable to associates, and managers, directors, and leaders of DS organizations [4].

II. HISTORY

During 20th century there were some serious adverse events associated with medical products and drugs that resulted in the development of pharmacovigilance.
1847- Sir James Simpson discovered chloroform as powerful anesthetic introduced in clinical practice.
1848- 1st milestone 169 years ago, young girl Hannah Greener of North England died receiving chloroform anesthesia before removal of an infected toe nail.
1937- 107 deaths in USA because of sulfanilamide elixir containing diethyl glycol.
1938- Federal Food, Drug and Cosmetic Act (FD&C Act) was enacted which began to examine the safety of new drug and risk profile of medical product, making a major step forward in drug safety regulations.
1950- Aplastic anemia reported due to chloramphenicol toxicity.
1961- Thalidomide tragedy milestone in the development of pharmacovigilance [5].
- It was said that history of PV is older than drug thalidomide, practically the history of PV starts from “thalidomide tragedy”.

- Thalidomide was sedative and hypnotic used in 1960.
- Swiss Pharmaceutical Company, CIBA originally developed the drug in 1953.
- German Pharmaceutical Company, Chemi Grunenthal introduced the drug as Contergan in 1956.
- It was widely used throughout the world as anti-emetic and was the first choice of drug by physician for morning sickness in pregnant women.

1964- Yellow card was introduce in Europe.
1965- Thalidomide stimulate the development of European Legislation [6].
1966- A Pilot study Boston collaborative Drug Surveillance Program.
1968- WHO program for international drug monitoring was instituted and 10 members
Participated (Australia, USA, UK, Germany, Canada, Ireland, Sweden, Denmark,
New Zealand and Netherland) [7].
1995- European Medicine Agency was setup.
2001- Eudravigilance was founded.
2012- Amendment in European pharmacovigilance [8].

III. AIM

- To improve patient care and safety in relation to the use of medicine and all medical and paramedical intervention.
- To improve public health and safety in relation to the use of medicine.
- To contribute to the assessment of benefit harm, effectiveness and risk of medicine encouraging their safe rational and more effective use [9].
- To promote understanding education & clinical training in pharmacovigilance.

Importance of safety monitoring
International drug monitoring began in 1968 with Uppsala monitoring center (UMC) Sweden being the collaborative center this global initiative.

Function:
Communication of safety signal recognized through analysis of global data.
WHO Promotes pharmacovigilance at country level.
At the end of 2020, 127 countries were the part of WHO pharmacovigilance program in 1998.
Importance of Drug Monitoring Safety

1. Drug safety monitoring is Mitigation exercise in which ADRs caused by therapeutic drug biological or devices can be explore, prevent or minimized.
2. It is essential elements for the effective use and high quality medical case.
3. It has potential to inspire confidence and trust among the patient and healthcare professional in medicine and contribute to rising standard of medical practice.
4. PV is the process of identifying expected and unexpected adverse reaction resulting from the use of medicine in the post marketing phase.
5. PV benefits everyone and patients are protected from unsafe drug.
6. Analysis of ADRs data help to make regulatory decision.
7. Prevent drug related damages if appropriate case is taken by physicians on the basis of feedback from the PV system [10].

Increased Necessity of Drug Safety Monitoring
There are multiple reason for the increased necessity for drug safety monitoring identify expected and unexpected ADRs result from the use of medicine in the post marketing phase. It is a risk mitigation exercise in which ADRs cause by the therapeutic drug, biological or device can explore, prevent or minimized. Before releasing to the market a medicine is tested with a limited population ranging 500-5000 [11]. Once the medicine comes into the market it become legacy available for consumption by the general population. The population may be children, pregnant women, patient suffering from other disease and elderly, It may be given separately or in combination with other medicine. Thus drug taken in different therapeutic situation and physiological condition, It is very much necessary to observe and record the effectiveness and safety of medicine the real life situation. A close and effective monitoring is required to assess the risk associated with the use of medicine. In fact adverse effect interaction with drug (other) or food and other risk factor are notice only during the real use over the year [12].

Need of Pharmacovigilance

I. Limitation of clinical study data
II. Withdrawal from market as a result of spontaneous reporting.

Ex. 1. Practolol caused blindness [Approved in 1970 and withdrawal in 1975].
2. Benoxaprofen which caused renal, liver and bone marrow toxicity [Approved in 1982 and withdrawal in 1983] [13].

Need of AI in Pharmacovigilance

In developing countries, photovoltaic technology remains a relatively novel concept with limited adoption. Countries all across the world are concerned about the necessity of post marketing safety monitoring programs [14].

PV was created primarily to protect patients who are only occasionally exposed to therapeutic medications during research and clinical trials. PV is responsible for evaluating, communicating, and assessing the risks and efficacy of these drugs.

Following the introduction of a new medication to the market, drug safety is now a serious concern. Unpredictable toxicities that result in morbidity and mortality from a typical dosage of the medication are the main cause of erosion during clinical trials or after marketing [15].

99 small molecule medications (67.8%) and 47 biologics (32.2%) were among the 107 therapies for 146 additional new indications that the FDA approved between 2017 and 2019. Of these, 74 (50.7%) had at least one special regulatory review designation, with 12 (8.2%) being reviewed under RTOR and 50 (64.1%) being designated for priority review. Of these, 78 (53.4%) were cancer medicines. Twelve (24.0%) of the 50 selected for priority evaluation were also granted RTOR approval [16].

PV practices can be significantly improved by AI and intelligent automation. These tools can automate routine processes such as repeating searches, verifying important regulatory data, and doing an initial quality check on individual case safety reports [ICSRs]. They can also rate instances for further analysis and assess the validity of instances to expedite signal discovery. They can also reduce the workload for pharmacovigilance specialists, allowing them to focus on other crucial tasks [17].

Possibilities for PV using AI

AI has had a big influence on pharmacovigilance.AI has the potential to improve medication safety decision-making by improving the quality of data collected from drug research [18]. Developments in image recognition and natural language recognition have made it easier to analyze large volumes of unstructured data, such as social media posts and clinical notes.[4] This capability allows for faster identification of adverse drug reactions and trends, ultimately leading to more informed regulatory decisions and enhanced patient safety. Patient safety is further bolstered by AI algorithms that can predict potential medication errors before they occur, allowing healthcare professionals to intervene proactively.[19] As AI technology continues to evolve, its integration into pharmacovigilance processes promises to create a more robust system for monitoring drug safety and efficacy in real-time. possible. Cloud-based pharmacovigilance platforms and ongoing developments in big data analytics will enable advanced analysis of large datasets. AI can speed up the risk assessment process and help reduce human error [20].

AI is able to search through huge amounts of data for trends and patterns that might improve human decision-making. Given their quick development, there are many opportunities to apply AI in pharmacovigilance. They are looking for an integrated system that would allow them to handle pharmacovigilance. From start to finish, the sector uses automation and hidden data to improve efficiency.[21]

The importance of AI in PV

There has been a lot of interest in the use of artificial intelligence (AI) in pharmaceutical development and life cycle management, including pharmacovigilance (PV). PV is described by the US Food and Drug Administration as "all analytical and statistical collection activities." referring to the identification, assessment, and awareness of undesirable circumstances." As well as individual case safety reports (ICSRs), clinical pharmacology studies, registries, and other, The FDA defines pharmacovigilance overall covering a number of scientific Studies.[22]

The FDA is looking into how artificial intelligence might be utilized within various of these sectors, but the research in those sectors has not yet grown enough for comprehensive legislation. The following criteria led us choose this remarkable topic.

a) ICSRs have been utilized for years to recognize security hazards and still remain important sources of latest safety information. After a drug is authorized, new safety problems usually assist.[23]

b) The quantity of ICSRs is analyzed, dropped, and modified for industry and regulatory bodies for safety indications as the number of data sources that require to be monitored investigated to collect safety information expands and separate. This imposes extra

pressure on some security experts and raises expenses. This general ability was identified by an increase in the reporting of drugs used to prevent and treat coronavirus disease 2019 (COVID-19).[24]

c) World regulatory bodies and standardization techniques require ICSR delivery. Improve productivity.

d) Despite the increased interest in safety recognition and evaluation, ICSRs are bound to continue to provide an important role as an early warning system for drug safety signals, especially for unusual occurrences, and will continue to be an important part of the photovoltaic industry for the foreseeable future. indication taken from population-based data sources' estimates.[25]

e) The current ICSR reporting processes were modified, but it appears unresolved that these modifications will be enough on their own.

Advantages of AI in PV

1. Reduced cycle times are the primary advantage of AI. The processing is spontaneous as an outcome of this technique.
2. Make the information more accurate and of higher quality.
3. AI has the potential of handling and managing many different kinds of incoming data forms.
4. It can be utilized for ADR identification.
5. AI can assist in minimizing the workload and analyzing time for cases.
6. Without the need for human intervention, AI systems analyze the case validity and extract data from adverse drug event forms.

AI has an extensive variety of uses in PV and will undoubtedly affect the field's bottom line [26].

Challenges of Using AI in PV

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 used for other reasons without the participants' consent.[27]

There exist many issues with Al's use in pharmacovigilance:

- Data Standardization and Quality:

Challenge: Pharmacovigilance require a wide range of knowledge sources that involve electronic health records, clinical trials, social media, logs, and spontaneous repetitions. These data are commonly unstructured, not adequate, or inconsistent.

Overcome: Conform to defined data formats (e.g., MedDRA, WHO Drug Dictionary) and use robust and healthy data preprocessing techniques, such as natural language processing (MLP) for text mining [28].

- Dynamic Nature of Pharmacovigilance:

Challenge: Pharmacovigilance must alter to new treatments, fluctuating threats and evolving rules and regulations, which can be troublesome for static Al models.

Overcome: The remedy is to build customizable Al systems that can continually gain knowledge and update the models with recent data. Implement enables real-time monitoring and feedback.

- Privacy and Ethical Issues:

Challenge: Using patient data for Al training raises ethical and privacy issues, particularly when it comes to private medical data.

Overcome: Ensure obedience to privacy laws (e.g., GOPR, HIPAA). Encrypt patient data through the application of both authentication and encryption methods.

- Regulation and Compliance Issues:

Challenge: Strict pharmacovigilance norms established by regulatory organizations like the FDA and EMA must be followed by al systems. Verifying the accuracy and legitimacy of Al models can be hard.

Overcome: Assist with authorities to draft straightforward rules regarding Al in PV. Deliver availability and correct verification research in 42 procedures for making decisions [29].

- Interpretability and Explainability:

Challenge: Since Mang Al models, notably deep learning models, operate as "black boxes," it can be tough to understand how they arrive at specific findings.

Overcome: Apply explainable AJ (XAI) techniques to shed light on model projections. Prioritize interpretable models if at all possible, and document your choices so regulators can look over them [30].

IV. CONCLUSION

For accurate ICSR processing in PV, AI techniques will now be useful in identifying and initiating a

concealed relationship. AI awareness is still growing in PV. Pharmaceutical and IT industries working together would be advantageous for medical device manufacturers and medications, could influence this consciousness by improving adherence to regulations, attaining financial savings, etc. Despite the existence of IT systems that streamline the processing of cases and these days, manual labor is still required for all stages of ADR reporting. encompassing case intake and data entry. Using AI, the complete procedure—from case receipt. It is possible to automate reporting. These processes will reduce expenses while simultaneously improving quality and accuracy. Raising knowledge about artificial intelligence (AI) in PV is crucial, as the majority of people were not aware of it until 2017 [31]. Some AI online applications, such "VigiAccess" for ADR statistics are accessible to the general public. AI-assisted automated input for PvPI techniques could reduce the amount of effort involved in the entire process, from receiving cases to reporting them. These processes will reduce expenses and improve quality and accuracy. The automated Globally, statistics are standardized, and UMC Sweden can monitor the data collected by different PV centers.

Medication safety measures may ultimately become more complex with the use of AI technology. Further research in the field of AI is needed with regard to PV. Although research on AI, databases, and tools is still in its infancy, these technologies have the potential to greatly advance PV technology [32].

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