REVIEW ON BASICS OF ARTIFICIAL INTELLIGENCE IN THE ADVANCEMENT OF ADVERSE DRUG REACTION PROCESSING

[1]Karthikeyan A, [2]Venkateswaramurthy N

[1]Intern Pharm.D, [2]Professor and Head
JKK Nattaraja College of Pharmacy

***Abstract*- The World Health Organization (WHO) defines ADR as "an unpleasant, unexpected reaction to a medical substance that occurs at levels usually employed in man for disease prevention, diagnosis, or therapy, or for the restoration, correction, or modification of physiological function." Artificial intelligence (AI) can assist to reduce case processing costs while also improving PV activities. Artificial intelligence is the use of digital technology to build systems capable of doing tasks that were previously thought to need human intelligence. Many manual pharmacovigilance procedures may be automated with the introduction of RPA (Robotic process automation), cognitive computing, and machine learning. MODEL MECHANISM: Neural networks, also known as artificial neural networks (ANNs) or simulated neural networks (SNNs), are an area of machine learning that serve as the basis for deep learning models. Deep learning, an artificial intelligence (AI) subclass of machine learning, has emerged as a promising and highly effective approach for merging and analysing diverse biological data sources in order to generate fresh ideas. With the evolution of electronic health records, a growing body of research has looked at the use of machine-learning techniques to the construction of disease models, probabilistic clinical risk assessment models, and practice-based therapy pathways. AI, databases, and tools are farther along in their development, and their use in PV is feasible in the future. Adoption of novel concepts aimed at enhancing the future of PV in order to improve patient medication safety.**

INTRODUCTION:

Pharmacovigilance (PV), the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem: It is still a prominent clinical and scientific subject. It continues to play an important role in addressing the challenges imposed by the growing range and strength of medications, all of which contain an unavoidable and often unexpected risk of harm.[1]. ADR is defined by World Health Organization (WHO) as ‘‘a response to a medicinal product which is noxious, unintended and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease or for the restoration, correction or modification of physiological function”.[2] When adverse effects and toxicity do occur, especially when previously unknown, it is critical that they are documented, assessed, and their relevance adequately conveyed to a community that is knowledgeable enough to evaluate the material. The major barriers are a lack of experience, funding, political support, and, most importantly, scientific infrastructure. Acknowledging these issues is critical for the future development of the science and practise of pharmacovigilance, since the reported incidence of adverse drug reactions in India ranges from 3.7% to 32.7%. A study conducted by Mysuru reported, 3.7% of hospitalised patients suffered an ADR. Furthermore, 0.7% of hospital admissions were related to ADR, with 1.8% of patients having fatal ADR.[3] and With PV budgets allocating 40% to 85% of spend on case processing and case volumes increasing at a pace of 10-15% per year,[4] taking cost out of case processing is the key target for 90% of survey respondents. Low-cost leaders are outsourcing, using scale, and aggressively optimizing case processing. According to the Individual Case Safety Report, survey respondents expect automation to deliver in an average yearly cost savings of 30%. (ICSR).[5] Artificial intelligence (AI) can help to minimise case processing expenses and enhance PV activities. The use of digital technology to construct systems that are capable of doing activities traditionally experienced to need human intelligence is known as artificial intelligence.[6] AI is structured differently; it is pre-programmed with problem-solving abilities. AI is also utilised in medical diagnostics, clinical settings to treat, detect, and forecast outcomes, search engines, and so on. It is also utilised in the health-care industry to monitor and prevent human health problems. There are opportunities for automation in all pharmacovigilance procedures, but the individual case safety report (ICSR) process was chosen for study due to its resource-intensive nature, risk of errors and operational inefficiencies. Moreover, adverse event reporting has grown significantly year over year. Much of this expansion may be related to the approval of new medications, the implementation of patient support programmes that increase the number of patient interactions, updating legislation, and a rise in the sources of adverse event reporting, such as social media and mobile medical apps. Traditional drug safety and electrical panels have delivered incremental innovation and limited automation, but the administrative cost of manually processing these adverse event reports remains significant. With the introduction of RPA (Robotic process automation), cognitive computing, and machine learning, there is a greater probability to automate many manual pharmacovigilance operations. Automation would not only save money, but it would also assist to decrease mistakes and enhance uniformity in information processing. The most significant benefit will be to patients from automation technologies of the ICSR process, which will improve safety signal identification and risk management.[7] The flowchart-based strategy utilizes integrating the process of history taking, which involves a clinician asking a series of questions and then arriving at a likely diagnosis by integrating the symptoms reported. Given the vast diversity of symptoms and disease processes encountered in everyday medical practise, this demands entering a huge volume of data into machine-based cloud networks.[8]

Cognitive services are a combination of natural language processing (NLP) and machine learning (Machine learning is an area of AI that gives computer systems the ability to learn without explicitly being configured) algorithms that aim to solve specific tasks

that would otherwise require human intelligence.[9] An annotated corpus, or material used to train the cognitive service, must be produced and developed in order to create cognitive services. The goal of this review was to provide an insight on ADR processing in future and establishing model prediction system in pharmacovigilance.
Only precise extraction of information on AEs, suspect drugs, patient information, and reporter information included in source documents allows regulatory agencies to identify genuine cases.

MECHANISM OF MODELS:
Neural networks, also known as artificial neural networks (ANNs) or simulated neural networks (SNNs), are a subfield of machine learning that provide the foundation of deep learning models. Their name and form are based on the human brain, and they replicate the way real neurons communicate with one another.
Deep learning, a subclass of machine learning in artificial intelligence (AI), has emerged as a promising and highly successful technique for combining and interrogating multiple biological data types in order to create novel hypotheses. Deep learning is widely employed in drug development and repurposing; nevertheless, its applications in ADR prediction using gene expression data are constrained.[10] When cognitive services are implemented into a production environment, the outputs of the services are subject to the assessment and feedback of a PV SME. This user feedback would be logged, examined, and quality verified before being passed back to the developer to further train and enhance the models. This enhancement might be realised by implementing incremental training of machine learning services on samples of fresh data points chosen by evaluating and recognising the error patterns of the outputs. Before releasing each feedback loop, the new versions of cognitive services would need to be validated. As a result, the validation framework be improved in the future with improved cognitive services as well. Adjustments to the assessment level may be made to the validation framework as the services improve and have a good AQL (Acceptable Quality Level) history.[9]

AI in ICSR processing is divided into two categories:
1. Input of both structured and unstructured content: enter information for reading the case through XML, DOCX, Image, and PDF. To extract ICSR information in a regulatory-compliant way, NLP and ML are employed.
2. AI for decision-making: ICSR is frequently not upto the quality. As a result, AI may play a vital role in developing unlisted or individual random AEs, drug predictors, relationship, and so on.[11]

Artificial Intelligence's Role in Pharmacovigilance:
1. The most significant advantages of AI are shorter cycle durations. The processing is spontaneous as a result of this strategy.
2. Improve information quality and accuracy 3. AI can handle or manage a variety of incoming data forms
4. It has the potential to be utilised to identify ADRs.
5. AI can assist in reducing the load and time required for case processing.
6. Without the workforce, AI algorithms gather information from the adverse drug event form and assess case validity.[11]

APPROACHES IN PHARMACOVIGILANCE PRACTICE:
AI is currently making breakthroughs into the public health sector and will have a significant influence on all aspects of primary care. Automation of adverse event (AE) case processing with artificial intelligence (AI) provides a chance to influence the most significant PV cost driver. With the advancement of electronic health records, a growing body of research has investigated the use of machine-learning techniques to the development of disease models, probabilistic clinical risk stratification models, and practice-based therapeutic pathways.[12]
Rather of looking for an ideal value, Bayesian neural networks train the model weights as a distribution. This increases their robustness and helps them to generalise with less overfitting. The Bayesian confidence propagation neural network (BCPNN) will be a very great asset to the expert evaluation of a large number of spontaneously reported ADRs.[13]
Study conducted by researchers has effectively trained and validated AI models for recognising ADRs and grading severity using unstructured text data from countrywide patient reports. Gradient boosting (LGBM) and transformer-based algorithms produced comparable results for internal and external validation, owing to the individual strengths and limitations of the various data processing and classification methods.[14]
In addition, a research used the publicly accessible Open TG-Gates and FAERS databases to construct 14 deep learning models to predict adverse medication events. Certain models may be used to determine if a possible drug candidate is capable of causing these adverse effects.[15] Furthermore, alternative models for various ADRs may be developed using the same feature selection, model development, and tuning methods.

Also, the MSAM method outperformed the Bi-LSTM+Self-Attention method. Because the ADE corpus comprises basic material, the self-attention results are likewise quite high. As a result, the results, MSAM model on the ADE corpus do not differ significantly from the results of the self-attention mechanism.[17]

TABLE 01: Summary of prediction and early detection use cases with commonly used AI approaches	
Key use cases for artificial intelligence to reduce the frequency of adverse drug events: a scoping review	Neural network (n=17), random forest (n=17), decision tree (n=11), support vector machine (n=11), gradient boosting machine (n=7), k-nearest neighbours (n=6), Bayesian (n=5)
Predict therapeutic response (or non-response) to medications	Neural network (n=10), random forest (n=9), support vector machine (n=9), Bayesian (n=5)
Predict optimal medication dose or adaptive dosing	Bayesian (n=6), decision tree (n=5), k-nearest neighbours (n=5), neural network (n=5), random forest (n=4), support vector machine (n=4)
Predict most appropriate treatment options	No common models
Early detection	
Detect ADEs	Neural network (n=6), random forest (n=3)
Detect medication prescribing errors	Detect medication prescribing errors[16]

LOUIS et al. developed an AI pipeline that used a knowledge database and gradient boosting trees to learn to properly detect ADRs from unstructured patient records. If the performance gained is already intriguing, it may be enhanced, especially for ADR seriousness determination, which will be planned utilising larger and more diverse datasets. Such a method would allow automated pharmacovigilance systems to meet the growing need for ADR reporting processing.[18]

A study found that adopting comparable drug-ADR and target-ADR profiles, a random forest model may be used for medication repositioning and repurposing. To some degree, our gene target-ADR relationships reflect GWAS (genome-wide association study) results, but for adverse responses occurring in patients (ADRs) rather than quantitative features. These relationships might assist (de)prioritize medication candidates in the preclinical research stage based on their projected adverse effects. Moreover, their target-ADR interactions might aid progress human biology by predicting the human in vivo consequences of perturbing a protein target.[19]

A Study conducted by Susmitha S et al., explored that, even though the transcriptome profiles are
evaluated independently for each medication of interest, their methodology yields ADR estimates for using it in conjunction with every other drug for which gene expression data is available. The utilisation of transcriptome data minimises reliance on preexisting knowledge of protein and pharmacological targets, which is often insufficient. In future study, it would be interesting to compare the results of past research for common drug-pairs as an extra analysis.[20]
Nadir Yalçın et al., concluded that Although there are comparable research in their present literature, there is no high-performance risk score as a web-tool for assessing ADR occurrence and severity in newborns. It is predicted that by using the generated risk score in clinical practise, patients at high risk of ADRs will be recognised and ADRs will be avoided before they occur. Furthermore, with a newborn-centered approach, doctors' knowledge of these medicines may be increased via a web-tool, and mitigation methods (change of drug, dose, treatment duration, etc.) can be explored based on a benefit-harm link for suspected substances.[21]

CONCLUSION:

More study in the field of AI about PV is required. AI, databases, and tools are at a more advanced state of development, and their progress in the field of PV is possible in the future. Adoption of innovative ideas targeted at improving the future of PV to enhance the safer use of medications in patients. The majority of research have been published in recent years, reflecting a burgeoning area of study, and we anticipate many more investigations in the coming years. The availability of new forms of data and access to unstructured EHR notes might propel the industry forward.

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