VOLUME - 12, ISSUE - 03, MARCH - 2023 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Biological Science

PHARMACOVIGILANCE –A SHORT REVIEW

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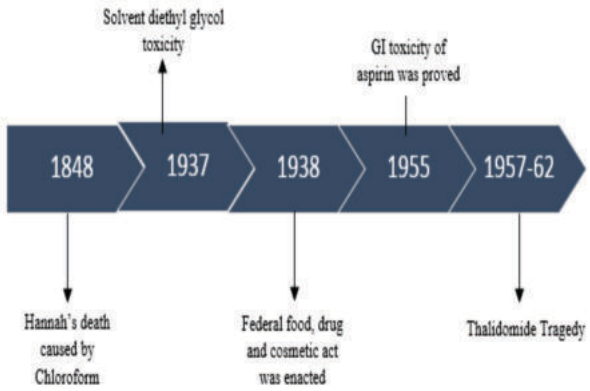
KEYWORDS :

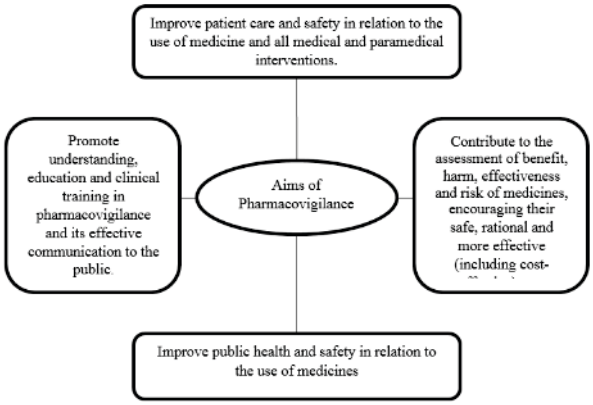
INTRODUCTION

The history of pharmacovigilance began on January 28, 1848. Hannah Greener, a young girl from northern England died after being injected with chloroform (Anaesthetic) before ingrowing toenail treatment. Chloroform was introduced into clinical practice by Sir James Simpson. The cause of Hannah's death was investigated and it was found to be due to fatal arrhythmia. Following other deaths and warnings by clinicians and the public about the safety of anesthetics, the Lancet Journal established a committee to address the issue. The commission called on British doctors, including Colonial Doctors, to report deaths from anesthesia. The United States Federal Food and Drug Act was enacted on June 30, 1906, and required that drugs be pure and uncontaminated.In 1937, 107 deaths were caused by the use of the elixier sulfanilamide which contained diethyl glycol as a solvent which is believed to be the cause of deaths, but the manufacturing companies were not aware of its toxicity. In 1938, the Federal Food, Drug, and Cosmetic Act was enacted. This law requires manufacturers to submit evidence of a drug's safety to the FDA before it can be marketed. In 1938, Douthwaite reported that aspirin could cause malena. The toxicity study of aspirin have shown various outcomes. However, in 1955, it was proved that aspirin can cause gastrointestinal diseases.[1]

On 1st Oct 1957, thalidomide was introduced in market and widely used as sedative and in morning sickness treatment during pregnancy. On 18th Nov 1961 a German physician Widukind Lenz indicated that thalidomide drug has severe teratogenic effect like deafness, phocomelia. Later it was confirmed by many physicians around the world. Sooner the drug was proved to be a powerful teratogen, around 10,000 infants were affected all over the world. The thalidomide tragedy stimulated the development of pharmacovigilance reporting.[2]



The etymological roots for the word "pharmacovigilance" are: Pharmakon (Greek) – drug and Vigilia (Latin) – to keep watch. As per WHO Pharmacovigilance is defined as, "the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems."[3]



Pharmacovigilance plays a vital role in detecting, collecting, researching, assessing and evaluating enough information from physicians and patients about the adverse drug reactions (ADRs) of the medicines and however, despite all their benefits, evidences shows that ADRs of medicines are common, also preventable. In some countries, adverse drug reactions are among the top 10 causes of death. Many other problems are also related to pharmacovigilance, such as substandard or spurious drugs and medication errors. Medication errors such as abuse, misuse or overdose as well as exposure to drugs during pregnancy and lactation are also important because they can lead to adverse drug reactions. In addition, if multiple medications are prescribed, there is always a risk of negative interactions. In addition, due to differences in gene profiles, a patient may respond differently to a drug and develop different side effects. A prime example is acute hemolysis that develops in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency when exposed to a commonly prescribed antimalarial drug, primaquine.[4]

Drug safety monitoring is essential at all stages of the drug life cycle.[5]

-Phases	Safety Investigated
Pre-clinical phase	To identify the safe dose in humans and to identify safety parameters for clinical monitoring.
Phase I	To estimate the tolerability of the dose range required for further clinical studies in healthy volunteers.
Phase II	Determine the appropriate dose range in patients with the disease or condition of concern.
Phase III	To improve understanding of a drug's benefit-risk profile and to identify less common side effects.
Post-marketing	Plays a key role for better defining the safety of drugs once they reach the market.

During the preclinical and clinical development of the drug, minimal safety information of the product is known. Continuous observation and evaluation is essential in clinical practice and a strong pharmacovigilance system is essential

to monitor this. Both clinical trial safety and post marketing pharmacovigilance are critical throughout the product lifecycle. Drug safety monitoring and risk management are extremely important to safeguard public health. To promote the safe use of medicines, a thorough evaluation of the new evidence generated by pharmacovigilance is required. The ultimate goal of pharmacovigilance is to promote rational and safe use of drugs, minimize risks associated with drug use, and maximize benefits.[4]

Classical examples of serious and unexpected adverse reactions.[6]

Drugs	ADR
Aminophenazone (amidopyrine)	Agranulocytosis
Chloramphenicol	Aplastic anaemia
Clioquinol	Myelooptic neuropathy (SMON)
Erythromycin estolate	Cholestatic hepatitis
Fluothane	Hepatocellular hepatitis
Methyldopa	Haemolytic anaemia
Oral contraceptives	Thromboembolism
Practolol	Sclerosing peritonitis
Reserpine	Depression
Statins	Rhabdomyolysis
Thalidomide	Congenital malformations

Uppsala Monitoring Centre (UMC), located in Uppsala, Sweden, is the field name for the World Health Organization Collaborating Centre for International Drug Monitoring. UMC works by collecting, assessing and communicating information from member countries' national pharmacovigilance centres in regard to the benefits, harm, effectiveness and risks of drugs.

Pharmacovigilance In Healthcare Emergency

During the early stages of the pandemic of Coronavirus disease 2019 (Covid-19), the lack of vaccines and drugs to treat/prevent COVID-19 led to a rush to re-use approved drugs for other indications. Due to an urgent need for an effective drug and vaccine against Covid-19, many currently available drugs, including antimalarial drugs such as hydroxychloroquine, and chloroquine, antiviral drugs such as lopinavir/ritonavir or remdesivir or favipiravir, antitoxin drugs such as ivermectin, immunomodulatory drugs such as corticosteroids, and monoclonal antibodies such as tocilizumab or sarilumab being added to treat COVID-19. It is essential to promptly and accurately record the adverse events for the safe use of drug therapy in patients.[5,7]

Hydroxychloroquine and chloroquine are quinolone derivates. Behavioral and mood disturbances such as psychosis, anxiety and irritability have been described for decades as possible side effects of quinolines. When patients have undergoing psychiatric condition, antimalarial medication put them at risk of worsening their psychiatric symptoms. In Morocco, and since the beginning of the epidemic, confirmed cases of COVID-19 have been systematically used a combination of hydroxychloroquine or chloroquine and azithromycin as first-line treatment.[8]

CASE -1

A 46-year-old male patient tested positive for COVID-19 and was given a chloroquine-azithromycin combination. The patient had a history of mild depression and had been treated with vortioxetine since November 2019. He has an ECG every two days. showed a normal to prolonged QT interval. On the 9th day of treatment, the patient showed symptoms of grief and insomnia. In the evening of the same day, he showed a sudden onset of psychotic symptoms such as visual hallucinations and incoherent speech, outbursts of strange behavior, and repeated attempts to flee the hospital. Several laboratory tests were performed, such as ionogram, blood count, serum glucose, creatinine, HIV, Syphilis serologies, etc., which turned out to be normal. So the decision was made to interfere with the COVID-19 medication protocol as well as vortioxetine and give amilsulpride at the dose of 100 mg per day. Psychotic symptoms disappeared totally after 2 days, and amisulpride stopped within a week. The patient showed no psychotic symptoms.[8]

CASE 2

A 35-year-old female patient tested COVID-19 positive and received a chloroquine-azithromycin combination, with no history of psychosis. After 3 days of the treatment, she had symptoms of insomnia, palpitations, a feeling of not being able to control her thoughts, distress, etc. Two days after these symptoms, the chloroquine-azithromycin combination is stopped and switched to a hydroxychloroquine-azithromycin combination. The patient followed this treatment for 6 days and showed no symptoms. Regarding psychiatric side effects, hydroxy chloroquine appears to be less risky than chloroquine.[8]

When all the evidence was against the use of HCQ, an observational study in India showed the benefits of HCQ prophylaxis for healthcare professionals. Subsequently, ICMR established a national task force for COVID-19, recommending that it should only be used in high-risk cases and only be given on the prescription of a registered pharmacist. The patients are advised to contact the health care professionals in case of any adverse events.

The above scenario of HCQ demonstrates the importance of pharmacovigilance in any drug therapy or drug discovery. In trials, HCQ had mixed results or even showed no benefit, but it posed an increased risk of adverse events or drug interactions that could worsen a patient's condition.[7]

COVID Vaccines – Adverse Events

As of June 19, 2021, 78 candidate vaccines are developed in 201 different ongoing trials. Of these, 12 vaccines have been approved by the US FDA, the World Health Organization (WHO), and the European Medicines Agency. Vaccine safety monitoring is essential to prevent serious risks and to improve patient's safety. Due to the lack of rigorous data from long-term studies on the safety of COVID-19 vaccines, there is an urgent need to strengthen post-market surveillance of adverse event data, especially in low- and middle-income countries. For the COVID-19 vaccines, the WHO Programme for International Drug Monitoring publishes a safety surveillance guideline that specifies a number of standards that must be met. Vaccine safety monitoring is key to improving safety records and building public trust. [9]

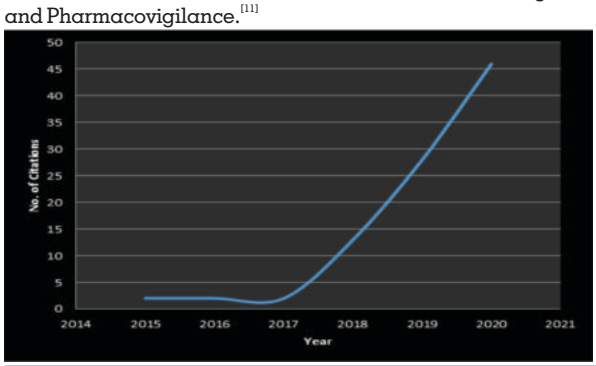
Adverse events related to COVID-19 vaccines in clinical trials.[9]

Vaccine	Adverse events
BNT162b2	Common: Fever, fatigue, headache, injection site pain. Serious: Shoulder injury related to vaccine administration, right axillary lymphadenopathy, paroxysmal ventricular arrhythmia, myocarditis and right leg paresthesia, fatigue and headache.
mRNA-1273 By Moderna	Common: Fever, headache, fatigue, myalgia, chills, and injection-site pain Serious: No serious adverse reaction
AZD1222 by Oxford/ AstraZeneca	Common: Headache, nausea, myalgia, arthralgia, injection-site tenderness, injection-site pain, injection-site warmth, injection-site pruritus, fatigue, malaise, feverishness, chills Serious: Pyrexia, transverse myelitis, hemolytic anemia
Sputnik V by Gamaleya	Common: Injection-site pain, fever, muscle pain, headache, asthenia Serious: No serious adverse reaction
Ad5-nCoV by CanSino	Common: Injection-site pain, rash, headache, muscle soreness, and fever Serious: No serious adverse reaction
Covaxin	Common: Fever, headache, fatigue, nausea, Vomiting Serious: Not reported
BBIBP-CorV	Common: Fever, fatigue, injection-site pain Serious: No serious adverse reaction
CoronaVac	Common: Injection-site pain Severe: Urticaria
Covishield	Common: Fever or chills, cough, shortness of breath, fatigue, muscle or body aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea or vomiting, diarrhea Serious: Not reported
Ad26.COV 2. S by Janssen	Common: Injection-site pain, headache, myalgia, fatigue, fever Serious: hypotension, bilateral nephrolithiasis in a patient with a history of kidney stones, legionella pneumonia, worsening of multiple sclerosis, fever leading to hospitalization

Artificial Intelligence In Pharmacovigilance

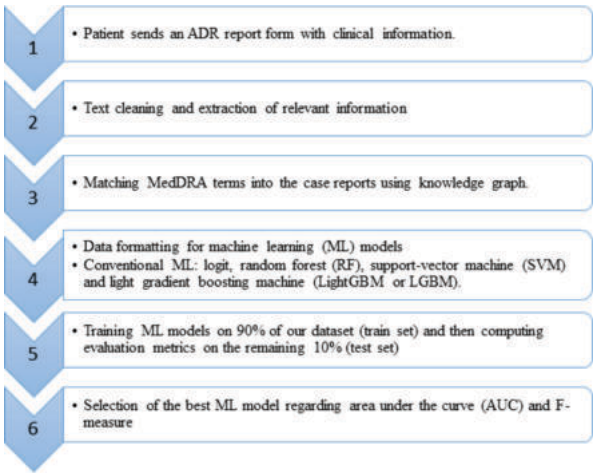
As per John McCarthy, father of Artificial Intelligence- It is the science and engineering of making intelligent machines. In short, AI is a next generation technology which we can replace manual activity to automatic business process without any human intervention.[10] AI is increasingly used in pharmacovigilance. The scope of Artificial Intelligence in Pharmacovigilance (AIPV) is even more essential due to the intertwined and overlapping fields of AI, machine learning (ML), deep learning (DL), data mining, and cognitive computing.[11]

Based on MEDLINE search for the terms Artificial Intelligence and Pharmacovigilance.[11]



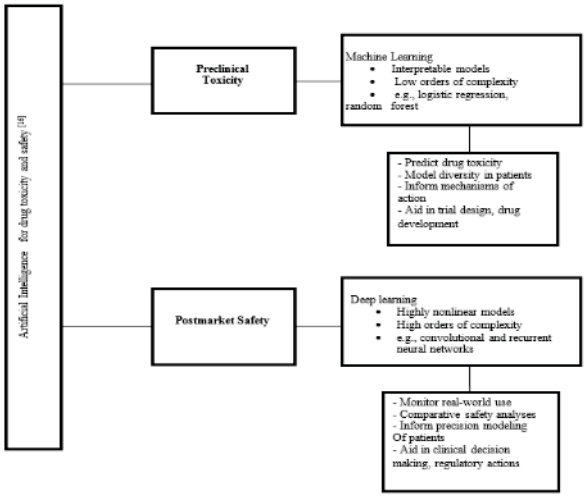
Processing pharmaceutical safety cases through automation offers a major chance to influence the biggest expense for a company's entire pharmacovigilance budget. The use of AI approaches in the field of biomedicine has grown in the past ten years.[12] Data is the key to Artificial Intelligence(AI) technology. As a result, it is crucial to create an extensive PV database. When developing their PV database, every nation is in a different scenario. In general, HCPs frequently start PV with ICSRs that are reported voluntarily. The Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS) and the Vaccine Adverse Event Reporting System (VAERS) in the United States, the Pharmacovigilance database in France, China's pharmacovigilance system, and VigiBase, are just a few examples of the numerous large-scale databases for PV or PV systems that have been developing in both developed and developing nations. The Uppsala Monitoring Center is in charge of maintaining VigiBase, which has data from more than 150 different nations.[13]

Artificial intelligence system for identifying and encoding adverse drug reactions (ADRs) from free text using MedDRA terminology.[14]



With the help of Artificial Intelligence and Machine Learning, there will be more clarity on a successful outcome. In order to predict biopsy-proven cancer and distinguish between normal and abnormal screening exams, IBM and others performed a retrospective machine learning analysis of mammography pictures. The authors asserted that their system could detect missed breast cancer diagnosis by a significant margin and could score breast cancer at a level "equivalent with radiologists."

Identifying risk groups for osteoporosis, monitoring adherence to anticoagulant medication, controlling TB, and forecasting asthma exacerbations are more instances of the application of AI in healthcare.[15]

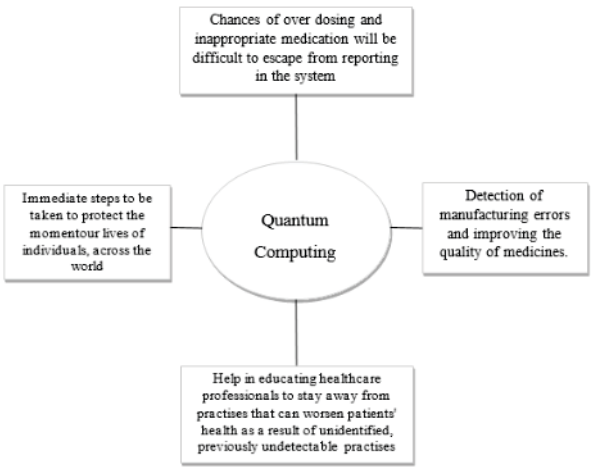


WHO Drug Koda on Adverse Drug Event Reports

WHO Drug Koda is one of the first drug coding engines using artificial intelligence. Koda can automatically code large proportions of drugs, including ambiguous drug names, using its internal coding rules and additional information about the drug, such as route, indication and country. With the use of optional, user-provided extra drug information, WHODrug Koda, an AI-powered drug coding engine, is designed to automatically code drug verbatims to WHO Drug Global entries. WHO Drug Koda was first created for the goal of coding concurrent medicines in clinical trials, but it may also be used in the coding of drugs reported in adverse event reports for postmarketing surveillance. Using a dataset of reports from VigiBase, Koda was able to achieve a 46% increase in automation over the basic baseline with no help from humans. Koda provides great automation levels and coding quality for drug coding of AE data in VigiBase even though it was created for concurrent drug coding in clinical trials. To ensure excellent data quality while automating and supporting coding standards during case processing for pharmacovigilance, Koda can be a useful tool.[17]

Quantum Computing In Pharmacovigilance

The recently established idea of quantum computing truly gives computers superhuman abilities and intelligence, which will not only help to lower healthcare costs but will also help to raise the standards and capacities of healthcare practitioners around the world. Artificial intelligence-driven sensors and patches will make it easier to record any adverse events in a patient's body and report them to a pharmacovigilance specialist who can keep a careful eye on any adverse events or responses brought on by the usage of both traditional and novel medications. Effective preventive measures must be taken in order to significantly lower the number of patient mortalities and morbidity brought on by pharmaceutical errors. Quantum computing will aid in the effective and efficient identification of ADRs and ADE. The use of quantum computing will improve all aspects of pharmacovigilance, which will strengthen efforts to serve patients and people around the world with high-quality medical care. [18]



Quantum Computing — A New Feature In The Pharmacovigilance Solutions For Drug Discovery

Computational methods for drug discovery are not new, but the use of super-efficient quantum computers to discover previously unknown molecules has recently emerged as a promising area. Quantum computers use "qubits," which can be on, off, or both, as opposed to conventional computers, which use "bits" that can only be either on or off. This is a phenomena known as superposition. This superposition capability of quantum computers makes the technology very appealing for efforts to identify new drugs by considerably accelerating and improving testing and projections.

A German-Australian company called Quantum Brilliance is working to make drug discovery powered by quantum mechanics a reality. The startup, founded in 2019, develops quantum diamond accelerators capable of simulating multi-molecular interactions for in silico drug development. Their goal for 2022 is to demonstrate the idea and value of distributed quantum computing (QC) for computational chemistry as part of their software stack. Although QC is still in its infancy, industry players have realized its potential to revolutionize medical research, and the recent wave of collaborations between QC teams and major pharmaceutical companies shows that pharmaceutical industry wants to participate.

In January 2022, Boehringer Ingelheim announced a partnership with Google Quantum AI to leverage quantum technology for in silico drug modelling. The pharmaceutical company Roche established a partnership with Cambridge Quantum Computing a month later in order to accelerate the creation of early-stage Alzheimer's disease medications.

The convergence of patient-generated health data, healthcare provider information, and machine learning models enables medications to deliver unique insights at previously inconceivable speed and scale. These insights go beyond drug safety and efficacy to include quality of life variables that can aid in pharmacovigilance improvements. The development of new therapeutic materials and pharmacovigilance solutions could benefit from quantum systems outperforming classical processors of equivalent size, weight, and power in similar environments. The use of digital technologies enables pharmaceutical companies to significantly improve the efficiency, speed, and quality of their pharmacovigilance programmes.[19]

Advanced Therapy Of Drugs Using Pharmacovigilance

Advanced therapy medicinal products (ATMPs) constitute an innovative class of heterogeneous research driven biopharmaceuticals.[20] Advanced therapy medical products (ATMPs) are increasing the likelihood of treating serious diseases, many of which now have no cure.[21] 939 ATMP clinical trials were being conducted in different disease areas between 1999-2015. Almost a quarter of trials involving ATMP were developed for cancer treatment and 19.4% of trials involved cardiovascular diseases. ATMP is one of the areas of growing interest. There are 21 studies in combined Phase II/III and 65 trials in Phase III.[20]

Due to the novelty, specially designed and harmonised laws are required to provide a high degree of health protection, as well as to harmonise and promote market access. There will frequently be a need to revise the regulations pertaining to ATMPs as we gain more experience and with the formation of the Committee on Advanced Therapies (CAT).

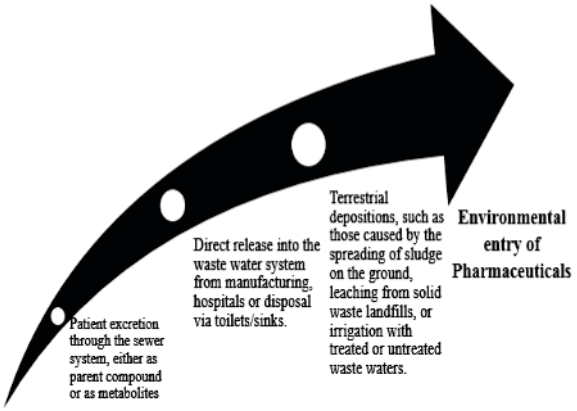
All medications used in advanced therapies must adhere to the regulations for post-authorization surveillance (pharmacovigilance) of pharmaceuticals for human use. Volume 9A of the Rules regulating Medicinal Products in the European Union contains comprehensive instructions that are taken from the law that establishes these regulations.

The European Medicines Agency, the European Commission, marketing authorization holders, national responsible authorities for medicinal products, and health care providers are all directly affected by the Community system of pharmacovigilance. National law may impose additional pharmacovigilance requirements on healthcare providers, distributors, pharmacies, clinical trial sponsors, non-commercial investigators, and ethical committees. Patients, healthcare professionals, academics, the pharmaceutical industry, and governments make up the major stakeholder groups.

It is anticipated that a risk management system with particular post-authorization studies will be required for the majority of ATMPs. Due to the novelty and high speed of growth in this sector, applicants are recommended to seek scientific guidance for Risk Management Planning. Currently, all medicinal products containing new active ingredients submitted through a centralized authorization procedure must provide a description of the risk management system, unless otherwise stated. A risk management framework, including specialised post-authorization studies, is expected to be sought for the majority of ATMPs. Due to the novelty and rapid pace of development in this area, candidates are urged to get scientific guidance from the European Medicines Agency (EMEA) for Risk Management Planning. [22]

Ecopharmacovigilance

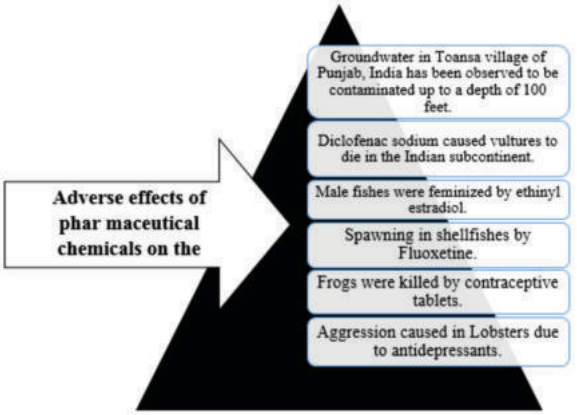
Ecopharmacovigilance (EPV) can be defined as science and activities concerning detection, assessment, understanding, and prevention of adverse effects or other problems related to the presence of pharmaceuticals in the environment, which affect human and other animal species. [23] A thorough Environmental Risk Assessment (ERA) is now a regulatory obligation prior to the launch of each new drug as a result of concerns expressed in recent years over the potential impact of pharmaceuticals in the environment (PIE). Reducing the danger of pharmaceutical pollutants harming the environment is a top priority for ecopharmacovigilance. Human medications, in contrast to many other substances that enter the environment, are made to interact with their intended biochemical targets in their intended target species in extremely particular ways. [24]



Environmental risk assessment (ERA) of pharmaceuticals is addressed by,

$$ERA = \frac{\text{Predicted environmental concentration (PEC)}}{\text{Predicted no-effect concentration (PNEC)}}$$

Both PV and EPV are intended to monitor drug side effects, PV in patients and EPV in the environment but can also occur in humans through indirect non-therapeutic exposure. [24] Industries utilise sewage treatment before disposal, however drug pollution of the environment remains due to outdated techniques. Few medications are not completely eliminated by the treatment procedure, leaving remnants in the environment's water. Some examples are cocaine, oral contraceptives, carbamazepine, and iodine contrast media. Cocaine has been discovered in the Po River in Italy. Antidepressant medications, carbamazepine and other antileptics, and lipid-regulating medicines (statins) were found in the Niagara River. In addition to these, there are numerous examples of medications discovered in aquatic environments. Ivermectin, an anthelmintic used in veterinary medicine, is excreted in the faeces and so has a negative impact on other creatures such as the dung beetle. [23]



Approximately 300 of the 4,000 pharmaceutical substances used in the medical industry have been found in drinking water systems before and are frequently found in aquatic environments with concentrations ranging from ng/L to g/L. To prove safety in the context of environmental effects and studies on the drug's effects over time, a mandatory provision may be established in the medicine development process. An Environmental Risk Assessment (ERA) must be completed before a medication is authorised for sale in India. [25]

In the Indian subcontinent, diclofenac is a commonly available veterinary medication that is used to treat and manage the symptoms of inflammation, fever, and/or pain brought on by illness or injury in domestic animals. When vultures devour the carcasses of cattle that were given diclofenac just before they died, they are exposed to the medication. Gyps vultures exhibit widespread visceral gout after experimental exposure to diclofenac or tissues contaminated with diclofenac, and they pass away within days from kidney failure. Gyps vulture carcasses from all around India, Pakistan, and Nepal had these clinical symptoms and diclofenac residues in the vulture tissues. Since the early 1990s, the populations of the Oriental white-backed (Gyps bengalensis), long-billed (Gyps indicus), and slender-billed vultures (Gyps tenuirostris) have decreased by more than 95% and are still declining at a pace of 22% to 48% per year. [26]

The frog species, Xenopus tropicalis is an excellent model for studying the developmental and reproductive toxicity of hormone-active chemicals. In X. tropicalis, the tadpole stage is crucial for the development of the reproductive system and gonadal differentiation. Due to the fact that the majority of amphibian species have an aquatic tadpole stage, it is also an exposure period of ecological relevance. Consequently, at this extremely important stage of development, amphibians may be exposed to waterborne environmental contaminants. Tadpole exposure to the synthetic progestin Levonorgestrel (LNG) severely disrupted the development of the oviduct and ovaries, resulting in the infertility of female X. tropicalis frogs. [27]

Drug use has become an inevitable part of our lives but it is not imperative to compromise with the balance of ecosystem on any grounds. Solutions need to be suggested to save this only livable planet from ill effects of these chemicals. These may include better sewage treatment plants, education over rational use of drugs, and development of biodegradable products. Biopharmaceuticals may be an alternative but we still lack a scientific evidence to accept them as a complete substitute of drugs in practice.

A mandatory provision may be made in the process of drug development to establish safety in the context of environment and a study of the impact of drug over environment. Environmental Risk Assessment (ERA) has become

mandatory before seeking market authorization of drugs in European Union (EU). We should, however, remember that the results of ERA are affected by several factors like dose of the drug used, characteristics of drug, metabolism of drug, biodegradation, measured environmental concentration, and ecotoxicity. It is also difficult to predict the chronic hazard potential of a drug in subacute concentrations on the basis of acute toxicity studies.[27,28] Countries like United Kingdom have witnessed the impact of stringent regulations. The American Senate has also passed a legislation to monitor the drugs in environment. As stated above, a number of Governmental and nonGovernmental organizations have also taken initiatives. Few of them are proving to be benchmark for international stakeholders, for example, in Nepal aviaries are being constructed following their success in Pinjore, India. But India with a multifold (almost 150 times) contamination as compared with developed countries is still striving for a robust system to safeguard the environment. Attention is paid to the culprit drugs only after the alarming episodes are reported. It will now be pertinent for regulatory as well as scientific society to work hand in hand to address this vital issue.

CONCLUSION

Clearly, the development of these massive sources of data for future pharmacovigilance efforts creates an opportunity for capitalizing on recent advances in deep learning and anomaly detection. A continuously learning artificial intelligence system could not only learn to integrate these heterogeneous data sources for real‐time ADR detection, but could help identify potential cases and interface with members of the pharmacotherapy community to gather more information when needed. The field of pharmacovigilance is rapidly evolving, however, the resources we have highlighted are only part of the solution; the FDA and National Institutes of Health (NIH) will need to continue their funding of research that focuses on how to effectively analyze these data streams. Ideally, funding mechanisms will ensure interdisciplinary teams of experts from epidemiology, sociology, statistics, and computer science among others. Collaborative interdisciplinary efforts will ensure both institutional buy‐in as well as methodological rigor. Ultimately, the combination of various data sources and expertise will result in safer and more effective pharmacotherapy for everyone.

Abbreviations	Definition
PV	Pharmacovigilance
FDA	Food and Drug Administration
WHO	World Health Organization
ADR	Adverse Drug Reaction
QPPV	Qualified Person for Pharmacovigilance
UMC	Uppsala Monitoring Centre
NPC	National Pharmacovigilance Centers
CDSCO	Central Drugs Standard Control Organization
HCQ	Hydroxychloroquine
AIPV	Artificial Intelligence in Pharmacovigilance
ML	Machine Learning
DL	Deep Learning
FAERS	FDA Adverse Event Reporting System
VAERS	Vaccine Adverse Event Reporting System
RF	Random forest
SVM	Support-Vector Machine
LGBM	Light Gradient Boosting Machine
AE	Adverse Event
ADE	Adverse Drug Event
QC	Quantum Computing
ATMPs	Advanced therapy medicinal products
EMEA	European Medicines Agency
CAT	Committee on Advanced Therapies
EPV	Ecopharmacovigilance
ERA	Environmental Risk Assessment
PIE	Pharmaceuticals In the Environment
PEC	Predicted environmental concentration
PNEC	Predicted no-effect concentration
NIH	National Institutes of Health
LNG	Levonorgestrel

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