ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 06, 2023

ADVANCED PHARMACOVIGILANCE TECHNIQUES, SOFTWARE, AND FUTURE PERSPECTIVES

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ABSTRACT

Pharmacovigilance starts with the clinical stage and continues the entire drug's life cycle. Pharmacovigilance is concerned with the evaluation, identification, and avoidance of potential drug-related issues and side effects, with a focus on the acute and long-term impacts of pharmaceuticals, biological products, herbal remedies, and conventional therapies. Pharmacovigilance has changed over the past few years as clinical practice and public health science have become more and more important. Pharmacovigilance employs a number of techniques, including targeted clinical investigation, stimulated reporting, passive and active surveillance, comparative observational studies, and descriptive investigations. The most recent advancements in pharmacovigilance are crucial to meeting patient needs and maintaining their health. The Erica Manifesto for Global Reform of the Safety of Medicines in Patient Care, Waller and Evans, and the Erica Declaration on Transparency are the three publications in pharmacovigilance that provide guidelines for the future. In order to persuade the patient that the medication should be used safely, pharmacovigilance in the future needs to be able to identify safe issues quickly. Furthermore, pharmacovigilance techniques can be utilized to determine whether patients are susceptible to adverse drug reactions (ADRs) and how those reactions might occur. The utilization of patients as information sources in the field of pharmacovigilance will be crucial for this process. The majority of ADR administration and reporting tasks involve software. The programs that are most frequently utilized include repClinical, PvNET, Oracle Argus Safety, ArisG, and Oracle adverse event reporting. Quality Control Test Results, Regulatory Management, Marketing and Sales Data Handling, Clinical Trial Data Management, etc. Sometimes, single software is used and sometimes a combination of two or more is used. The

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pharmaceutical industry as a whole uses about nineteen different types of software, each of which has a vast range of products from numerous vendors. Currently, there has been a slight increase in the use of the program following the implementation of GMP, GLP, and GCP.

Keywords: *Adverse effects, Reporting, Pharmacovigilance, Active surveillance.*

INTRODUCTION

Pharmacovigilance is the study, identification, and avoidance of potential drug-related issues and side effects, with an emphasis on the acute and long-term impacts of pharmaceuticals, biological products, herbal remedies, and traditional treatments. It is crucial to the decision-making process in pharmacotherapeutics. [1].

It encourages the sensible and safe use of medications by:

- Improving the prompt discovery of medication interactions and ADRs that were not previously known.
- Identifying the risk factors for ADR development.
- Sharing information to enhance medication prescription and regulation.[2]

Pharmacovigilance starts in the clinical stage and continues the entire drug's life cycle. [3]

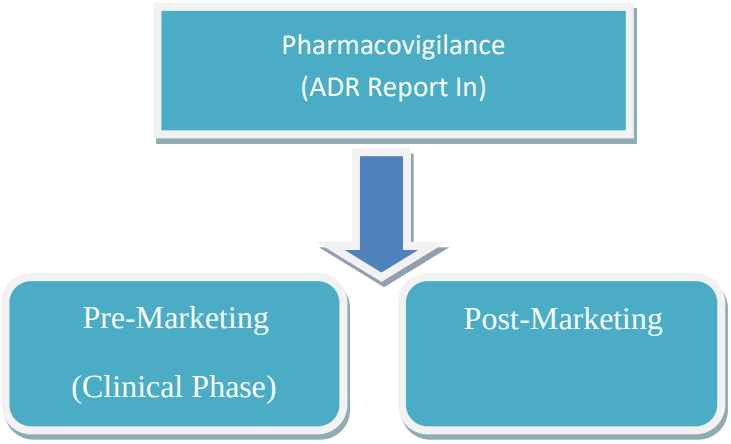

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Fig-1Pharmacovigilance ADR Report

Pharmacovigilance has changed in recent years due to the growing significance of improved clinical practice and public health science. However, there are many obstacles facing the field of pharmacovigilance today as it strives to create a better healthcare system worldwide.

Following are the major challenges faced in the pharmacovigilance:

- Broader safety concerns
- Assessment of established products
- Economic growth in public health versus pharmaceutical industry
- Web-based sales and information.[4]

PHARMACOVIGILANCE METHOD

Fig:-2Pharmacovigilance Method

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PASSIVE SURVEILLANCE: This pharmacovigilance technique, a type of spontaneous reporting system, places healthcare workers in charge of identifying and starting the process of reporting an adverse drug response (ADR). The most widely used reporting method is believed to have been defined as:

- Effortless
- Cheapest among all the methods.

Nevertheless, this spontaneous method has a very low reporting rate when compared to other approaches. In districts where there is not enough funding or staff to conduct active surveillance, spontaneous reporting can be carried out using National ADR reporting forms. [5]

ACTIVE SURVEILLANCE: A proactive approach is adopted to pinpoint the unfavorable incidents. The patient's follow-up following medication is the foundation of this pharmacovigilance approach. The following are ways to identify adverse drug reactions:

- Asking the patients directly.
- Screening of the records of patients.[6]

STIMULATED REPORTING: Health practitioners are encouraged to report new goods using this approach. The reporting method consists of:

- Online reporting of adverse events
- Systematic stimulation of adverse events.[7]

COMPARATIVE OBSERVATIONAL STUDIES

The primary purpose of these research is to validate the signals obtained from case series or unprompted reports. It is a conventional approach to assessing adverse medication occurrences.

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Studies on pharmacokinetics and pharmacodynamics are carried out. Whenever risk factors are found in pre-approval clinical studies, additional trials are conducted to assess the mechanism of action [8].

8]

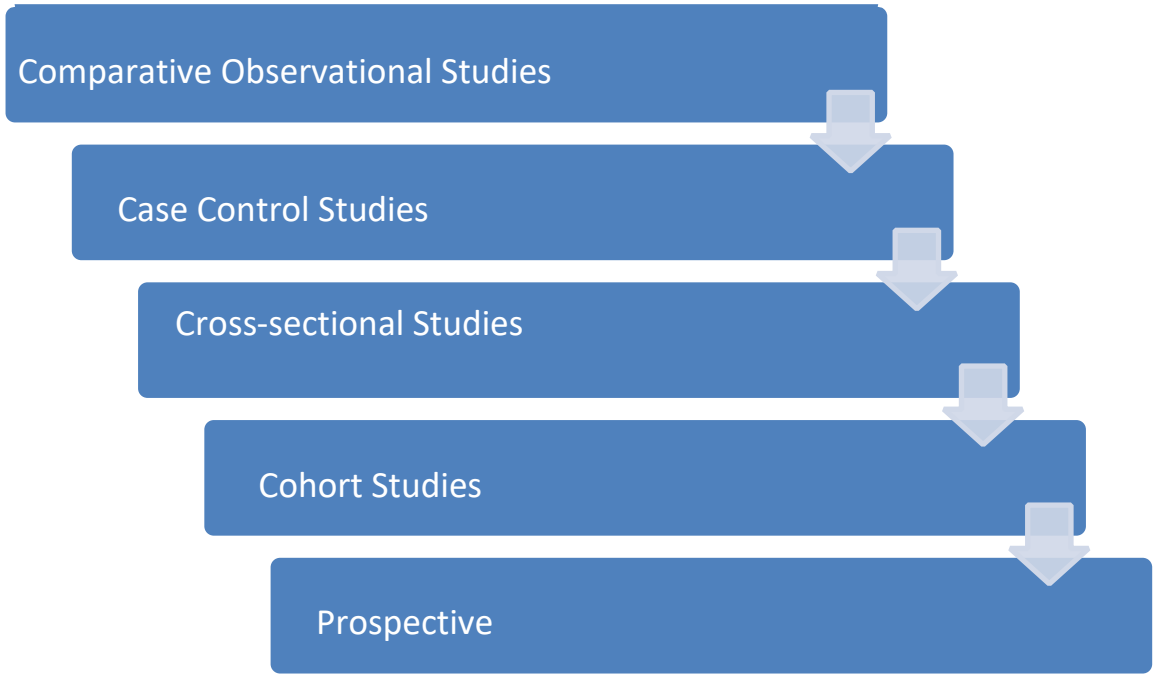

Fig: 3 Comparative observational Studies

RECENT DEVELOPMENT IN THE FIELD OF PHARMACOVIGILANCE

New advances in pharmacovigilance are critical to meeting patient needs and maintaining their health. Three pharmacovigilance publications are available for future guidance. The three publications include:-

1. The Erice Declaration on Transparency, which contains the following claims:

- Information about drug safety must be made available to the public in order to support their health.
- Distributing information regarding extra safety information or the proper and safe use of the drugs to as many members of the public and healthcare professionals as possible.

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- Every piece of proof needs to be readily available and thoroughly evaluated in order to comprehend the advantages and disadvantages.
- Every nation needs to have a system with independent expertise in order to guarantee that data regarding the safety of all medications is available and is gathered, then assessed.
- To ensure that issues are correctly and efficiently discovered and that remedies are effectively communicated, new advancements in medication safety monitoring are necessary. [2]

2. Eric Manifesto, which calls for worldwide reform of the safety of pharmaceuticals used in medical care include the following are:

- Public and patient involvement in the discussion of the advantages and disadvantages of medications as well as in the process of making decisions on their own care should be active.[9]
- There need to be innovative approaches to gather data regarding the efficacy and safety of medications designed to facilitate the gathering, examination, and sharing of data, a candid dialogue needs to be carried out and end with a decision.
- Learning how to enhance pharmacovigilance techniques should go hand in hand in hand with official, professional, and public cooperation.
- Pharmacovigilance has been shown to benefit the public, legislators, officials, scientists, physicians, patients, and the general public must all support it.[10]

3. Waller and Evans

Their opinion on how pharmacovigilance should be carried out going forward was expressed.

The key values for pharmacovigilance are:

- Excellence is the best outcome that can be achieved.
- The scientific method
- Transparency.[11]

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SOFTWARE USED IN THE FIELD OF PHARMACOVIGILANCE

There are much software which is used in pharmacovigilance are:-

- Oracle Argus Safety
- Aris G
- MedDRA
- PVNET
- Artificial Intelligence
- Oracle Adverse Event Reporting
- RepClinical

1. ORACLE ARGUS SAFETY

This all-inclusive platform is mostly utilized to meet pharmacovigilance standards. Pharmacovigilance is currently dealing with issues such as a rise in case volume, complicated business, difficulty analyzing safety data, and inconsistent data sources. As a result, it's made to control the requirements. Argus safety offers the following benefits:-

- Tracking of local data items
- Risk management capabilities
- A product’s benefit: risk profile
- Duplicate search capabilities
- Improve safety of drug [12]

Pharmaceutical companies, contract research organizations (CROs), and regulatory agencies around the world use Oracle Corporation's Argus Safety Database, a software application for pharmacovigilance and drug safety management. It is made to gather, organize, and analyze adverse event data from clinical trials, post-marketing surveillance, and spontaneous reports. Advantages of Argus Safety Database are:-

- Scalability
- User-Friendly Interface
- Data Entry
- Manage ADR

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- Case Processing Event[13]

Argus Safety Database allows users to manage adverse events efficiently. It offers case processing, reporting, and data entry facilities. The system supports several languages and can process massive amounts of adverse event data. Potential safety signals can be found using the integrated signal detection and management feature of the Argus Safety Database. The system uses advanced statistical methods and algorithms to detect patterns and trends in adverse event data. [14]

2. Aris G

ArisG is a fundamental part of an integrated pharmacovigilance and risk management system that helps businesses keep an eye on their goods and proactively detect potential safety issues. ArisG advanced automated features and adjustable process assist expedite the management of adverse drug reactions. By automating the routing of cases according to workflow rules, users can more effectively build up a system that satisfies their business process and standard operating procedure (SOP) needs. Versions of ArisG are available both on-premise and on demand, just like all other Aris Global products. Software that pharmaceutical businesses use the most frequently has the capability needed to handle adverse event reporting. For the treatment of adverse medication reactions, ArisG makes use of sophisticated automation technologies and a customizable process. A fundamental element of the risk management system is established by ArisG; this allows for simple product monitoring and proactive identification of risk concerns by the businesses. Among the software programs used by pharmaceutical corporations most frequently for pharmacovigilance is

ArisG. [14]

More than 300 businesses globally that keeps their vital drug safety data in ArisG use it. All of the functionality needed to handle adverse event reporting and adverse reaction regulations set forth by various regulatory bodies worldwide is provided by ArisG. All pharmacovigilance procedures are supported, including CIOMS, Med Watch 3500A, and many more, from case input to the automatic generation of submission-ready adverse event (AE) reports.

3. MedDRA

The Medical Dictionary for Regulatory Activities (MedDRA) is a globally recognized pertaining to medical ailments, pharmaceuticals, and medical equipment. It was developed to make information

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sharing between regulators easier. Industry, academia, medical practitioners, and other groups that disseminate medical knowledge also use it. Both medical experts and non-medical professionals may report a safety report. [15]

MedDRA is widely utilized, including applications in the US, EU, and Japan. In Europe and Japan, its use is currently permitted for the purpose of safety reporting. ICH The MedDRA MSSO's operations are inspected by the MedDRA management board. Six ICH parties, Health Canada, the UK's Medicines and Health Care Products Regulatory Agency (MHRA), and the World Health Organization (as an observer) make up the management board. All phases of clinical trials, with the exception of animal toxicology, therapeutic indications (signs, symptoms, diseases, diagnosis, or prophylaxis of disease), modification of functions, coding names and quantitative results of investigations, surgical procedures, and medical/social/family history, are coded in medical terms using MedDRA. [16]

MedDRA USED

- Clinical Trial phase 1, Clinical Trial phase 2, Clinical Trial phase 3, Clinical Trial phase 4.
- Clinical study reports.
- Safety summaries and reports for specific cases.
- Investigator’s Broacher. Analysis.
- Marketing Applications.
- Publication.
- Prescribing information.
- Advertising.[17]

Languages of MedDRA

Previously, MedDRA was only available in English and Japanese. However, it is now available in multiple languages. They are as follows:

1. French
2. German
3. Italian

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4. Spanish
5. Russian
6. Korean
7. Chinese [18]

STRUCTURE OF MedDRA

There are five hierarchical levels of medical phrase coding in the MedDRA dictionary.

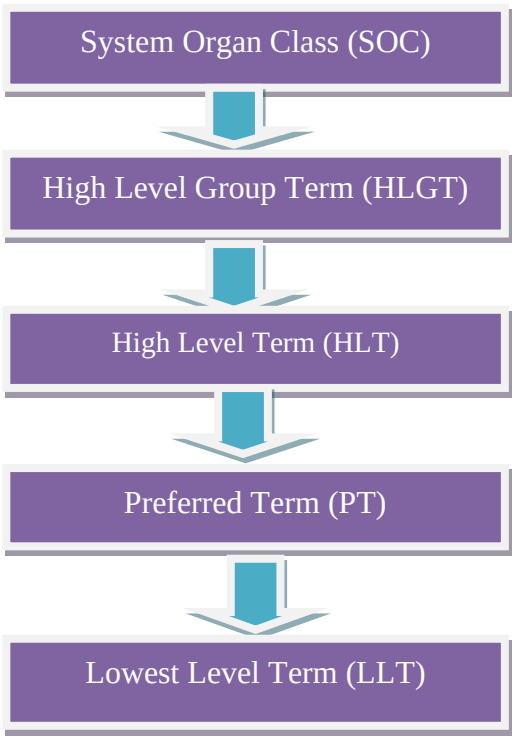

Fig: 4 Levels of MedDRA

4. PVNET

PvNET is a premier software program for pharmacovigilance, offering more than only compliance with its regulatory reporting of Individual Case Safety Reports (ICSRs), adverse event reporting, and adverse drug reaction (ADR) data management. PvNET assists in incorporating safety information across the entire development and marketing process, enabling users to make informed decisions. PvNET has passed audits for medication safety across the board that check for

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conformity with 21 CFR, GMP standards, and ICH E2B.PvNET aids in the integration of safety data, which in turn supports users' essential decision-making processes within the software. Add on modules allow for the addition of new features to it. One of the most crucial pieces of software for pharmacovigilance adverse drug event reporting, ADR data management, and creation and examination of numerous regulatory reports is this one. [12] PvNET has many features, such as:

- Process that facilitates the division of data entry, quality control (QC), and scientific evaluation/medical review.
- Cross-field validation checks and extensive data validation are used to verify case files for E2B compliance.
- Dictionary management (MedDRA version management) and worldwide dictionary support Records of audits for the management of safety data.
- Management Dashboard: This dashboard allows users to focus on pertinent domains and provides them with the necessary information to identify abnormalities and outliers, enabling them to take prompt action.
- Automated story writing for serious adverse events and multilingual text assistance.
- Duplicate case checking.
- Centralized triage before complete case handling

In addition to recording adverse events, PvNET has been designed to analyze and produce a range of regulatory reports, including:

- E2B compliant XMLs
- CIOMS
- Med Watch
- ICH approved periodic reports including PSURs, bridging reports and other annual reports.[14]

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5. ARTIFICIAL INTELLIGENCE

Artificial intelligence (AI) is the healthcare system is transforming the function of medical professionals and opening up new avenues for enhancing patient safety and treatment quality. In both inpatient and outpatient settings, artificial intelligence is being used to increase patient safety. By using digital techniques that facilitate communication between patients and their healthcare practitioners, it has also been utilized to reduce avoidable harm. [19]. Artificial intelligence is being more and more used in pharmacovigilance in a number of domains, such as signal management, target population identification, and safety operations. Artificial intelligence is primarily used in pharmaceutical research to identify adverse drug reactions (ADEs) and adverse drug events (ADRs); to perform surveillance and signal detection; to classify free text in safety reports; to extract drug-drug interactions; to identify high-risk populations for drug toxicity; to predict drug side effects; and to simulate clinical trials. These can be used in pharmacovigilance in a variety of contexts, such as adverse event profiles and individual case safety reports (ICSRs). [20]

BENEFITS OF AI

1. Shorter cycle times are AI's primary advantages.
2. Boost the information's precision and quality.
3. AI is able to process and handle a variety of incoming data formats.
4. It is applicable to ADR identification.
5. AI helps to lighten the workload and speed up the case processing procedure.
6. Artificial intelligence (AI) tools assess the case after extracting data from the adverse drug event form. [21]

6. Oracle Adverse Event Reporting

Managing your global safety information might be challenging, but Oracle AERS offers a single, all-inclusive solution with strong automation and productivity tools. Any medical product, including medications, medical devices, vaccines, biologics, and gene therapies, from both spontaneous and clinical sources, can have its significant adverse event and product compliance cases captured, managed, reported, and analyzed with Oracle AERS.

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Companies that produce biopharmaceuticals, vaccinations, medical devices, and Contract Research Organizations (CROs) have ongoing challenges in achieving stringent regulatory criteria on schedule with limited funding. Designed with ease of use by experts, Oracle AERS is accountable for the following:

Fig: 5 Oracles Adverse Event Reporting

Industry experts created Oracle AERS to be user-friendly for all users. The user-friendly interface offers strong capability at a button press. Users are able to visualize the case pieces and comprehend the overall case picture through the interactive presentation of crucial information provided by the AERS graphical user interface. Validated displays and basic end-user tools are used for configuration and administration. [14]

7. RepClinical

RepClinical assists you in efficiently and economically handling your vital pharmacovigilance tasks. RepClinical facilitates the collection of adverse event data, the creation of regulatory reports, and the sharing of ICSRs with various regulatory agencies and commercial partners. RepClinical offers clear interfaces and practical tools to make it simple to create accurateE2B reports. The data in Individual Case Safety Reports (ICSRs) and repClinical are closely modeled by each other. In

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instances, case data can be tracked and saved. One of the safest web-based services available, this program is primarily in charge of managing pharmacovigilance activities in an economical and efficient manner. It functions in an incredibly easy and efficient way. [12]

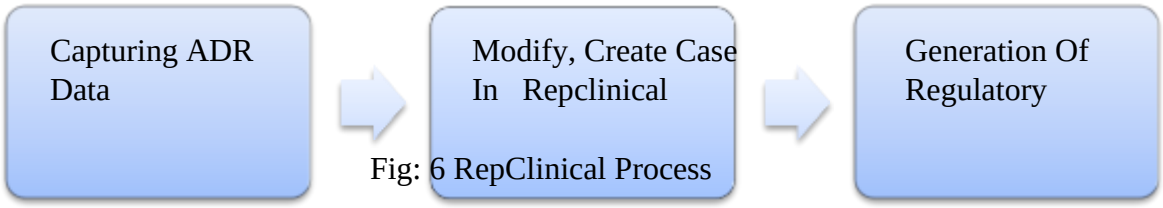

Fig: 6 RepClinical Process

FUTURE PERSPECTIVE

In order to elevate pharmacovigilance to the status of a science, it is imperative to create novel techniques that supplement the existing framework. During the post-marketing period of active surveillance, it is important to remember to collect information within a specific timeframe. This is because the purpose of active surveillance is to obtain information on the safety of drugs at an early stage of drug development. There aren't many reports accessible on spontaneous reporting, despite the fact that it was helpful in signal production. Consequently, a decrease in risk factor identification makes it more difficult to detect ADRs.In the past, patients had minimal engagement and were not particularly aware of the sickness; however, in the present, patients are well-informed about the illness and actively engage in therapy. Patients have the ability to report adverse drug reactions (ADRs) in several countries; this trend will continue in the future and serves as a valuable information source. [1] The strict discipline of observation contributes to the creativity required in this profession. In order to persuade the patient that the medication should be used safely, pharmacovigilance in the future needs to be able to identify safe issues quickly.

Additionally, pharmacovigilance techniques can be utilized to determine whether patients are susceptible to adverse drug reactions (ADRs) and how those reactions might occur. The utilization of patients as information sources in the pharmacovigilance sector is crucial for this process. With the emergence of new technologies and developments, software usage in the pharmaceutical industry is predicted to increase over the next several years.

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Software applications will be even more essential in promoting innovation and efficiency in the pharmaceutical sector as a result of the complexity of drug research and the rising demand for individualized medication. [7]

CONCLUSION

Software is now a vital tool in the pharmaceutical business. Software has completely changed the way pharmaceutical businesses run and greatly increased output, accuracy, and efficiency. Every step of the pharmaceutical value chain has changed as a result of software applications, including clinical trials, drug development, and regulatory compliance. Electronic Data Capture (EDC), Clinical Trial Management Systems (CTMS), Pharmacovigilance Systems, and Electronic Document Management Systems (EDMS) are a few of the major software programs used in the pharmaceutical industry. Applications from these businesses support data management, process optimization, compliance assurance, and better decision-making. With the emergence of new technologies and innovations, software usage in the pharmaceutical industry is predicted to increase over the next few years. Software applications will become even more important in propelling innovation and efficiency in the pharmaceutical industry, given the complexity of drug development and the growing demand for personalized medicine.

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