Review Article

A SYSTEMATIC REVIEW OF PHARMACOVIGILANCE AND ADVERSE DRUG REACTION

Gadkar Krishna Vishnu[1], Misal Shivani Santosh[2], Atole Chhaya Vinayak[3], Suke Janhavi Gorakh[4].
Navasahyadri Institute of Pharmacy Nasrapur Dist.Pune (412 213).

ABSTRACT:

The history of pharmacovigilance started back 169 years ago with the death of a 15- year-old girl, Hannah Greener. However, the Thalidomide incident of 1961 brought a sharp change in the pharmacovigilance process, with adverse drug reaction reporting being systematic, spontaneous, and regulated timely. Therefore, continuous monitoring of marketed drugs was essential to ensure the safety of public health. Any observed adverse drug reaction detected by signals was to be reported by the health profession. Moreover, signal detection became the primary goal of pharmacovigilance based on reported cases. Among various methods used for signal detection, the Spontaneous Reporting System was most widely preferred; although, it had the limitation of "under-reporting". Gradually, the World Health Organization Collaborating Centre and "Uppsala Monitoring Centre" were established in 1978 for international monitoring of drugs. The center was responsible for operating various databases like vigiflow, vigibase, vigilyze, and vigiaccess. Recently, huge data could be generated through spontaneous reporting linked with computational methods, such as Bayesian Framework, E-Synthesis. Furthermore, drug safety surveillance at an early stage prior to the official alerts or regulatory changes was made possible through social media. In addition, India created a National Pharmacovigilance Program, and Schedule Y of the Drug and Cosmetic Act 1945 was reviewed and amended in 2005.

Keywords: Pharmacovigilance, Adverse drug reactions, Uppsala Monitoring Centre, World Health Organization (WHO).

INTRODUCTION

The challenge of maximizing drug safety and maintaining public confidence is indeed complex. Pharmaceutical and biotechnology companies have the responsibility to monitor and proactively assess and manage drug risks throughout a product's lifecycle, from development to post-market. This involves implementing robust pharmacovigilance systems to identify and evaluate potential risks, conducting clinical trials to gather safety data, and adhering to regulatory guidelines and requirements. (1) Indeed, pharmacovigilance plays a crucial role in drug regulation systems, public health programs, and clinical practice. It encompasses the science and activities involved in detecting, assessing, understanding, and preventing adverse effects of drugs or any other potential drug- related problems. By actively monitoring and evaluating the safety profile of drugs, pharmacovigilance helps identify and mitigate risks, ensuring the overall safety and effectiveness of medications. It also facilitates the collection and analysis of data on adverse drug reactions, enabling regulatory authorities, healthcare professionals, and patients to make informed decisions regarding drug use. Ultimately, pharmacovigilance contributes to the improvement of patient safety and the optimization of healthcare outcomes. (2)

According to the World Health Organization (WHO), pharmacovigilance is defined as the science and activities involved in the detection, assessment, understanding, and prevention of adverse effects or any other possible drug-related drawbacks, particularly the long-term and short-term adverse effects of medicines. The term "pharmacovigilance" has its roots in the Greek word "Pharmakon," meaning "drug," and the Latin word "vigilance," meaning "to keep watch." It is important to note that pharmacovigilance is not a new concept in many Asian countries and has, in fact, been ongoing since 1998. This demonstrates the recognition of the importance of monitoring and ensuring the safety of medicines in these regions for over two decades. (3) When Asian nations decide to join the Uppsala Centre for Adverse Event Monitoring, they gain access to an important tool for gathering safety data through spontaneous reporting of adverse drug reactions and adverse events. This method allows for early detection of potential risks associated with drugs. While clinical trials are essential for establishing the safety and efficacy of a drug before it is commercially marketed, they do have limitations. Strict inclusion and exclusion criteria limit the generalizability of trial results to a selective group of patients. Special populations such as children, pregnant women, and elderly individuals are often not included in these trials, and factors like genetic variations, environmental influences, and

drug- drug interactions may not be fully studied during the clinical trial phase.

By actively monitoring and analyzing data on adverse events, pharmacovigilance enhances the understanding of drug safety profiles and helps improve patient care by providing valuable information for drug prescribing and regulatory decision-making (4) You are correct that adverse drug reactions (ADRs) can have significant negative impacts on patients, including increased suffering, morbidity, and mortality. These ADRs also impose a financial burden on society. The estimated overall incidence of ADRs in hospitalized patients is approximately 6.7%. Data suggests that patients who experience ADRs have a 19.18% higher death rate and an 8.25% longer hospital stay compared to those without ADRs. Additionally, the total medical cost for patients with ADRs is increased by an average of 19.86%. These statistics highlight the importance of effective pharmacovigilance and proactive management of drug risks to minimize the occurrence and impact of ADRs, ultimately improving patient outcomes and reducing healthcare costs. (5)

Its stated objectives were:
It is support and strengthen consumer reporting ofsuspected ADRs.
It expands the role and scope of national pharmacovigilance centers to identify,analyze and prevent medication errors.
It is promoted better and broader use of existing pharmacovigilance data forpatient safety.
It is developing additional pharmacovigilance methods to complement data fromspontaneous reporting systems.
The work was organized into four main themes:
Increasing patient reporting of problems associated with the use of medicines.
Collection by national pharmacovigilance centers of reports of medication errors.
Improving the use of available pharmacovigilance data for identifying drug dependence,
counterfeit and sub-standard medicines, and for clinical risk estimation.
Development of active and targeted spontaneous pharmacovigilance activities.

HISTORY OF PHARMACOVIGILANCE IN ASIAN NATION:

Table No.01 : Sequential Pharmacovigilance development with special reference to India (6)

Year	Developments
1747	Very first known clinical trial by James Lind, proving usefulness of lemon juice in preventing scurvy.
1937	Death of more than 1000 children due to toxicity of Sulphanilamide.
1950	Aplastic anaemia reported due to Chloramphenicol toxicity.
1961	Worldwide tragedy due to thalidomide toxicity.
1963	16th World Health congregation recognize significant to rapid action on AdverseDrug Reactions.
1968	WHO research project for International drug monitoring on pilot scale.
1996	Global standards level clinical trials initiated in India.
1997	India attached with WHO Adverse Drug Reaction Monitoring Program.
1998	Initiation of PV In India.
2002	67th National Pharmacovigilance Centre established in India.
2004-05	India launched National PV Program.
2005	Accomplishment ofstructured clinical trials in India.
2009-10	PVPI started.

The sequential pv developments shown in the above table.
In 1986, pharmacovigilance (PV) was initiated in an Asian nation with the establishment of twelve regional centres, each covering a population of 50 million. However, the progress made in developing a proper adverse drug reaction (ADR) monitoring system was not significant. In 1997, Bharat (India) joined the World Health Organization (WHO) and attempted to implement an ADR surveillance program based in two urban centres, but it was not successful. Subsequently, in 2005, the WHO provided support and the World Bank funded the National PV Program (NPVP) of Bharat, which became operational. This initiative aimed to strengthen the pharmacovigilance system in the country and improve the monitoring and management of adverse drug reactions. (7,8,9,10).

STEPS IN PHARMACOVIGILANCE PROGRAMME:

1. Finding the risk of drug
2. Clinical trials
3. Pharmaco epidemiological study
4. Case report
5. Developing case series
6. Analysis of case series
7. Use of data mining to identify product-event combination

PARTNERS IN PHARMACOVIGILANCE:

You are correct in highlighting the complex and vital relationship that exists between various partners involved in drug safety monitoring. Collaboration and commitment among these partners are indeed crucial for effectively addressing future challenges in pharmacovigilance and ensuring its continued development and success. This includes close collaboration between pharmaceutical companies, regulatory authorities, healthcare professionals, patients, and other stakeholders. By working together, sharing information, and pooling resources, these partners can enhance the detection, assessment, and prevention of adverse drug effects.

- Government
- Industry
- Hospitals and academia
- Medical and pharmaceutical associations
- Poisons information centres
- Health professionals
- Patients
- WHO

METHODOLOGY:

PHARMACOVIGILANCE IN INDIA:

In a country as vast as India, with a population of over 1.2 billion and significant ethnic and socioeconomic diversity, it is indeed crucial to have a standardized and robust pharmacovigilance (PV) and drug safety monitoring program (SMP) in place. The pharmaceutical industry in India is valued at $18 billion and is growing at a rate of 12-14% annually, with approximately 40% of generic medicines being exported worldwide. India is also emerging as a hub for global clinical research and drug discovery and development, with outsourced projects in pharmacovigilance.

The Central Drugs Standard Control Organization (CDSCO) in New Delhi has witnessed a significant increase in the total number of applications received and processed, doubling from 10,000 in 2005 to 22,806 in 2009. This reflects the introduction of new chemical entities (NCEs) into the country. Given the diverse disease prevalence patterns and the practice of different systems of medicine in India. By implementing such a program, India can ensure the timely detection, assessment, understanding, and prevention of adverse drug reactions and other drug-related problems. This will help safeguard the health and well-being of its population and contribute to the overall growth and development of the pharmaceutical industry in the country. (11)

History of PV in India:

Traditionally, there was no emphasis on monitoring the safety of medicines in the country. However, it is important to note that pharmacovigilance (PV) is not entirely new to India. In 1986, a group of physicians, primarily from academic institutions, recognized the need for increased attention to potential adverse effects of prescription medicines and rational prescribing practices. As a result, the first ADR monitoring program was established, consisting of 12 regional centres, each covering a population of 50 million. However, it is acknowledged that this initial program faced challenges and was not successful in achieving its objectives. Despite this setback, efforts have been made to strengthen pharmacovigilance in India over the years. The establishment of the Pharmacovigilance Programme of India in 2010, in collaboration with the WHO, has been a significant step towards improving ADR monitoring and reporting in the country.

While pharmacovigilance in India may still be considered in its infancy, ongoing efforts are being made to enhance the system and promote a culture of ADR reporting among healthcare professionals and the general public. These initiatives aim to ensure the safe and effective use of medicines and contribute to the overall improvement of public health in India. (12)

The establishment of the WHO ADR Monitoring Program in India in 1997 marked a significant step towards pharmacovigilance, aiming to monitor adverse drug reactions (ADRs) associated with medicines marketed in the country. However, despite the identification of three monitoring centres, including the National Pharmacovigilance Centre at AIIMS, New Delhi, and WHO special centres in Mumbai and Aligarh, the initiative faced challenges.

One of the main issues was the non-functionality of these centres, attributed to a lack of awareness among prescribers about the need to report ADRs and a general lack of information about the functions of the monitoring centres. Additionally, inadequate funding from the government contributed to the unsuccessful implementation of the program.

Recognizing the shortcomings, a renewed effort was made to strengthen pharmacovigilance in India. From January 1, 2005, the WHO-sponsored and World Bank-funded National Pharmacovigilance Program for India was made operational. This initiative aimed to enhance the monitoring of ADRs, improve reporting mechanisms, and address the challenges that hindered the earlier program's success.

The implementation of the NPVP reflected a commitment to safeguarding public health by systematically monitoring and addressing adverse reactions to medicines. Ongoing efforts in pharmacovigilance contribute to a safer and more effective use of medications in India. (13) The National Pharmacovigilance Program established in January 2005 in India had a comprehensive structure with the National Pharmacovigilance Advisory Committee overseeing its operations at the CDSCO. The program included zonal centres, regional centres, and peripheral centres to collate and report information on adverse drug reactions from across the country. Despite its well-defined structure and objectives, the program faced challenges. The program had three broad objectives:

1. Short-term Objective: Foster a reporting culture.
2. Intermediate Objective: Involve a large number of healthcare professionals (HCPs) in information dissemination.
3. Long-term Objective: Establish the program as a benchmark for global drug monitoring. The current PV program in India:

The decision to restart and revamp the National Pharmacovigilance Program in India was a crucial step in enhancing drug safety and monitoring adverse drug reactions (ADRs). The initiative took shape during a brainstorming workshop jointly organized by the Department of Pharmacology at AIIMS and CDSCO in late 2009. The outcome of this collaborative effort was the formulation of a new and revised program, now known as the Pharmacovigilance Programme for India.

The revamped PvPI aimed to address the shortcomings of its predecessor and overcome the challenges that hindered the effective implementation of the NPVP. The program was officially operational from mid-July 2010, signifying a renewed commitment to pharmacovigilance and drug safety in the country.

Key features and improvements in the Pharmacovigilance Programme for India may have included:

1. Enhanced Awareness and Training: Efforts were likely made to increase awareness among healthcare professionals about the importance of reporting ADRs. Training programs may have been implemented to equip healthcare professionals with the knowledge and skills needed to actively participate in pharmacovigilance activities.
2. Streamlined Reporting Structure: The reporting structure may have been optimized to ensure efficient collection and analysis of ADR data. This could involve a clearer delineation of responsibilities among various levels of the reporting network, including zonal and regional centres.
3. Increased Stakeholder Involvement: Collaboration between regulatory bodies, healthcare institutions, and other stakeholders may have been strengthened to ensure a more comprehensive and coordinated approach to pharmacovigilance.
4. Improved Communication Channels: Efforts to improve communication channels for disseminating information about ADR reporting, program objectives, and updates may have been a focus, addressing one of the challenges faced by previous programs.
5. Strategic Partnerships: Collaborations with international pharmacovigilance organizations, such as the Uppsala Monitoring Centre in Sweden, might have been reinforced to leverage global best practices.

The renaming of the program to PvPI might have signalled a fresh start and emphasized the commitment to building a robust pharmacovigilance framework in India. Continuous monitoring, evaluation, and adaptation based on real-world experiences are crucial for the sustained success of such programs. (14)

The Union Ministry of Health in India has appointed the Indian Pharmacopoeia Commission as the new National Coordinating Centre for PvPI. This change signifies a strategic decision to involve the IPC in the leadership role, highlighting its responsibility to oversee and coordinate pharmacovigilance activities across the country.

The main aim of the NCC at IPC is to generate independent data on the safety of medicines. This data generation is crucial for assessing the benefit-risk profiles of medications and ensuring that the safety monitoring standards align with global benchmarks. By appointing the IPC as the NCC, there is likely an emphasis on maintaining transparency, credibility, and international compliance in the pharmacovigilance processes.

Key responsibilities of the NCC at IPC may include:
1. Data Collection and Analysis: Systematically collect, analyse, and evaluate data on adverse drug

reactions (ADRs) from various sources to assess the safety of medicines.
2. Reporting to Regulatory Authorities: Provide timely and accurate reports on ADRs to regulatory authorities, contributing to evidence-based decision-making.
3. Collaboration with Stakeholders: Foster collaborations with healthcare professionals, institutions, and international pharmacovigilance organizations to enhance the efficiency and effectiveness of the program.
4. Training and Awareness: Conduct training programs and awareness campaigns to engage healthcare professionals and the public in pharmacovigilance activities.

METHODS OF CAUSALITY ASSESSMENT:

Assessing and categorizing ADRs is a complex process that involves the use of various criteria and methods to establish a relationship between the administration of a drug and the occurrence of an adverse event. Some of the commonly used criteria and methods include:
1. Temporal Relationship
2. Dose-Response Relationship
3. DE challenge and Challenge
4. Exclusion of Other Causes
5. Confirmation by In Vivo or In Vitro Tests
6. Literature Review and Previous Reports
7. Known Pharmacological Effects
8. Expert Consensus

By combining these criteria and methods, researchers aim to categorize ADRs into different classes of causality, such as certain, probable, possible, unlikely, or unrelated. This comprehensive assessment helps healthcare professionals, regulatory authorities, and researchers make informed decisions regarding the safety of drugs and patient care. (15)

However, researchers and healthcare professionals commonly use three broad classes of approaches for relation assessment:

1. Professional Judgment:
Professional judgment involves the subjective assessment of healthcare professionals, often relying on their clinical experience and expertise.
Pros: This approach allows for the incorporation of nuanced clinical knowledge and contextual information. Experienced clinicians may use their judgment to weigh various factors in determining the likelihood of a causal relationship.
Cons: Subjectivity can lead to variability between different assessors, and it may be influenced by individual biases. Lack of standardized criteria can make it challenging to replicate assessments.

2. Algorithms:
Algorithms involve the use of predefined sets of criteria and rules to systematically assess the relationship between drug exposure and ADRs. These criteria may include factors like temporal relationship, DE challenge, challenge, and exclusion of other causes.
Pros: Algorithmic approaches aim to provide a more standardized and reproducible method of assessment. They can be applied consistently across different cases.
Cons: Algorithms may not capture the full complexity of clinical scenarios, and their rigidity might overlook unique aspects of individual cases. They may also need periodic updates to reflect advances in medical knowledge.

3. Probabilistic Approaches:
Probabilistic approaches involve the use of statistical methods to quantify the probability of a causal relationship between drug exposure and ADRs. Bayesian reasoning is often employed in these approaches.
Pros: Provides a quantitative measure of the likelihood of causality. Can account for uncertainties and incorporate evolving evidence over time.
Cons: May require access to comprehensive and accurate databases for prior probabilities. The complexity of statistical methods may limit their application in routine clinical practice. (16)

PHARMACOVIGILANCE IN DRUG REGULATION:

Pharmacovigilance programs made strong by links with regulators. Regulators understand that PV plays a specialized and pivotal role in ensuring ongoing safety of medicine products. Clinical trial regulation involves the rules, standards, and processes set by regulatory authorities to ensure the ethical conduct, safety, and quality of clinical trials. These regulations are designed to protect the rights and well-being of study participants, maintain the integrity of trial data, and facilitate the development of safe and effective medical interventions. The specific regulations can vary by country, but they generally cover several key aspects: 1. Ethical Considerations:
Regulatory frameworks require that clinical trials adhere to ethical principles, including informed consent, voluntary participation, and respect for the rights and privacy of participants.
2. Good Clinical Practice (GCP):
GCP guidelines provide an international ethical and scientific quality standard for designing, conducting, recording, and reporting clinical trials.
3. Protocol Design and Approval:

Regulatory authorities typically require a detailed and well-structured protocol for each clinical trial. The protocol outlines the objectives, design, methodology, statistical considerations, and participant eligibility criteria.
4. Informed Consent:
Regulations mandate that participants provide informed consent voluntarily after receiving comprehensive information about the trial, its risks and benefits, and their rights. 5. Safety Reporting and Monitoring:
Adverse events and safety information must be collected, documented, and reported to regulatory authorities as specified in the regulations. Continuous monitoring of participant safety during the trial is essential, and mechanisms for reporting and managing adverse events are established.
6. Data Integrity and Recordkeeping:
Rigorous recordkeeping is required to ensure the integrity of trial data. Regulations specify the documentation and data management practices that must be followed.
7. Investigator Responsibilities:
Investigators conducting the trial must meet certain qualifications, adhere to the protocol, and ensure compliance with regulatory requirements.
8. Regulatory Submissions and Approvals:
Before initiating a clinical trial, sponsors typically need to submit applications to regulatory authorities for review and approval.
9. Post-Marketing Surveillance:
After a drug or medical intervention is approved, post-marketing surveillance requirements may be in place to monitor its safety and effectiveness in real-world conditions.

Post marketing safety drug monitoring:

Post-marketing safety drug monitoring, also known as pharmacovigilance, is a crucial aspect of ensuring the ongoing safety of pharmaceutical products once they are approved and available in the market. The primary goal is to detect and assess adverse drug reactions (ADRs) and other safety-related information that may not have been apparent during pre-marketing clinical trials. Here are key components of post-marketing safety drug monitoring:
1. Adverse Event Reporting:
Healthcare professionals, patients, and drug manufacturers are encouraged to report any adverse events or suspected side effects associated with a drug to regulatory authorities. 2. Signal Detection:
Signal detection involves the systematic analysis of reported adverse events to identify potential safety concerns or signals associated with a particular drug.
3. Risk Assessment and Management:
Risk management strategies may include updates to product labelling, communication of safety information to healthcare professionals, or, in extreme cases, withdrawal of the drug from the market.
4. Periodic Safety Update Reports (PSURs):
Marketing authorization holders are often required to submit PSURs to regulatory authorities at defined intervals. PSURs provide a comprehensive overview of the safety profile of a drug, including any new safety concerns and relevant risk-minimization measures.
5. Risk Communication:
Transparent communication of safety information to healthcare professionals, patients, and the public is a crucial component of pharmacovigilance.
6. Registry Studies and Observational Research:
Post-marketing studies, including registry studies and observational research, may be conducted to further evaluate the long-term safety and effectiveness of a drug in real-world settings.
7. Collaboration and Information Sharing:
Global databases and networks, such as the WHO Global Individual Case Safety Reports database, facilitate international collaboration in pharmacovigilance.
8. Continuous Benefit-Risk Assessment:
The benefit-risk balance of a drug is continuously assessed based on emerging safety data and evolving clinical knowledge. Decisions regarding labelling updates, risk minimization measures, or regulatory actions are made to ensure the ongoing safety of patients.

Pharmacovigilance in national drug policy and disease control public health program

Pharmacovigilance plays a crucial role in the development and implementation of national drug policies. National drug policies encompass a set of strategies, regulations, and guidelines established by a country to ensure the safe, effective, and rational use of pharmaceuticals within its healthcare system.
1. Monitoring and Surveillance:
Pharmacovigilance contributes to the monitoring and surveillance of ADRs and other safety related issues associated with pharmaceutical products.
2. Ensuring Drug Safety:
National drug policies often include provisions for ensuring the safety of medicines throughout their lifecycle.
3. Regulatory Decision-Making:
Pharmacovigilance data influence regulatory decision-making processes related to the approval, labelling, and post-marketing monitoring of drugs.
4. Incorporation into Healthcare Systems:
National drug policies often incorporate pharmacovigilance into the overall healthcare system, defining the roles and responsibilities of

healthcare professionals, regulatory agencies, and other stakeholders. This integration ensures that pharmacovigilance activities are seamlessly woven into routine healthcare practices.

5. Capacity Building:

National drug policies may include provisions for building and strengthening pharmacovigilance capabilities within the country. This involves training healthcare professionals, establishing reporting systems, and enhancing the capacity of regulatory agencies to conduct pharmacovigilance activities effectively.

6. Post-Marketing Surveillance:

Pharmacovigilance contributes to post-marketing surveillance efforts outlined in national drug policies. Continuous monitoring of the safety of marketed drugs allows for timely detection and response to emerging safety concerns.

7. International Collaboration:

Many national drug policies recognize the importance of international collaboration in pharmacovigilance. Countries often participate in global pharmacovigilance networks, share information, and collaborate on safety assessments to benefit from broader experiences and perspectives.

MEDICATION ERRORS:

Questionnaire on Medication Error Monitoring:

Designing a questionnaire on Medication Error Monitoring involves considering various aspects related to the identification, reporting, and prevention of medication errors. Below is a sample questionnaire that can be used as a starting point for gathering information on this topic. Adapt and modify the questions based on the specific context and objectives of your Medication Error Monitoring program.

Section 1: Respondent Information

1. Name (Optional):
2. Role/Position:
3. Healthcare Organization:
4. Years of Experience:

Section 2: General Understanding

5. How would you define an error in your practice?
6. How significant is the issue of medication errors in your healthcare setting? Section 3: Identification and Reporting
7. Are there established procedures for identifying and reporting medication errors in your healthcare facility?
8. Who is responsible for reporting medication errors in your healthcare setting? 9. What methods or systems are in place for reporting medication errors? Section 4: Analysis and Investigation
10. Is there a systematic process for analysing and investigating medication errors in your facility?
11. What factors are typically considered during the analysis of a medication error? Section 5: Prevention Strategies
12. What strategies or interventions are in place to prevent medication errors in your healthcare setting?
13. How often are staff members educated or trained on medication safety practices? Section 6: Suggestions for Improvement
14. Do you have any suggestions for improving the Medication Error Monitoring process in your healthcare facility?

THE ROLE OF PHARMACIST IN DRUG SAFETY:

Pharmacists play a crucial role in drug safety throughout the entire medication use process. Their responsibilities extend beyond dispensing medications to include various aspects of drug safety, patient education, and collaboration with other healthcare professionals. Here are some key aspects:

1. Medication Dispensing:

Ensuring Accuracy: Pharmacists are responsible for accurately dispensing prescribed medications, checking for drug interactions, contraindications, and ensuring the correct dosage.

2. Patient Counselling:

Education: Pharmacists educate patients on how to take their medications, including proper administration, potential side effects, and any necessary precautions. Addressing Concerns: Addressing patient concerns, questions, and providing guidance on the safe use of medications.

3. Medication Therapy Management:

Reviewing Medication Regimens, Monitoring Adherence

4. Medication Safety Monitoring:

ADR Monitoring: Pharmacists play a role in monitoring and reporting adverse drug reactions to relevant authorities. Identifying Medication Errors: Detecting and preventing medication errors, including incorrect doses, drug interactions, or other safety concerns.

5. Collaboration with Healthcare Providers:

Communication: Collaborating with physicians, nurses, and other healthcare professionals to ensure coordinated and safe patient care.

Consultation: Providing consultations to healthcare providers on medication-related issues and contributing to interprofessional discussions about drug therapy.

6. Pharmacovigilance:
Reporting Adverse Events: Actively participating in pharmacovigilance activities by reporting adverse events and contributing to the monitoring of drug safety on a broader scale. Risk Management: Implementing risk management strategies to minimize potential harm associated with medications.

7. Drug Information and Patient Advocacy:
Providing Information: Offering accurate and up-to-date drug information to both healthcare professionals and patients to support informed decision-making.
Advocacy: Advocating for patient safety and participating in initiatives to improve medication safety practices within healthcare organizations.

8. Continuous Professional Development:
Staying Informed: Keeping abreast of developments in pharmacology, drug safety, and best practices through continuous education and professional development.
Training and Education: Providing training to pharmacy staff and students on medication safety and adherence.

9. Community Engagement:
Public Awareness: Engaging with the community to raise awareness about safe medication practices and promoting the role of pharmacists in ensuring drug safety. Health Promotion: Contributing to health promotion initiatives, such as vaccination campaigns, to enhance public health and prevent diseases.

ADVERSE DRUG REACTION (ADRs):
Adverse Drug Reactions refer to unintended and harmful responses to a medication that occur at doses normally used for treatment. These reactions can range from mild to severe and may occur immediately after a drug is administered or after prolonged use.(17,18,19) 1. Types of Adverse Drug Reactions:
Type A (Augmented): Predictable and dose-dependent reactions that are an extension of a drug's pharmacological effects. Examples include gastrointestinal disturbances or bleeding associated with aspirin use.
Type B (Bizarre): Unpredictable reactions that are not related to the known pharmacological actions of the drug. These reactions are often idiosyncratic and may involve the immune system, leading to allergic reactions or hypersensitivity.
Type C (Chronic): Reactions that occur with long-term use, such as drug-induced endocrine or metabolic disorders.
Type D (Delayed): Reactions that manifest after a delay, often involving cumulative drug exposure over time.
Type E (End of Use): Reactions that occur upon discontinuation of a drug, such as withdrawal symptoms.
2. Factors Contributing to ADRs: Patient-related factors, Drug-related factors, Environmental factors, idiosyncratic reactions.
3. Common Adverse Drug Reactions:
4. Serious and Life-Threatening ADRs:
5. Monitoring and Reporting ADRs:
6. Prevention and Management:
7. Regulatory Actions:
Patient safety is at the forefront of ADR management and prevention strategies.

Table No.2:- Drug and its Adverse effect (20)

DRUGS	ADVERSE DRUG REACTION
Thalidomide	Phocomelia, Multiple Defects.
Methotrexate	Multiple defects, Fetal death.
Androgen	Virilization of limb, esophageal, cardiac defects.
Progestin	Virilization of female fetus
Stilbesteron	Vaginal carcinoma in teenage female offspring
Tetracycline	Discolored or deformed teeth, retarded bone growth
Warfarin	nose, eye and hand defects, growth retardation
Phenytoin	Various malformations
Lithium	Fetal goiter, cardiac and other abnormalities
Aspirin/Indomethacin	Premature closer of ducts arteriosus
Quinidine	Ringing in ear
Alcohol	Low IQ baby, growth retardation
Carbamazepine	Neural tube defects

Rifampicin	Orange color urine
Chloramphenicol	Grey baby syndrome.
Anticancer Drugs	Cleft palate, multiple defects.
Valproate Sodium	Spina bifida, limb abnormalities.
Isotretenoin	Heart and CNS defects.

Documentation of ADRs:
Documentation of Adverse Drug Reactions (ADRs) is a crucial aspect of pharmacovigilance to ensure systematic recording, monitoring, and analysis of adverse events associated with medication use. Proper documentation helps healthcare professionals, regulatory authorities, and pharmaceutical companies track and assess the safety of drugs. Here are key considerations for the documentation of ADRs(21):
1. Adverse Event Reporting Form:
2. Patient Information:
3. Suspected Medication(s):
4. Concomitant Medications:
5. Healthcare Professional Information:
6. Severity and Outcome:
7. Causality Assessment:
8. Follow-Up Information:
9. Regulatory Reporting Requirements:
10. Documentation System:

PROCEDURE FOR REPORTING ADRs:
It is the first duty of any pharmacovigilance centre to report all suspected adverse events of the drug if found. Information regarding ADRs that should be reported and tabulated.

Monitoring of ADRs:
The monitoring of Adverse Drug Reactions is a critical component of pharmacovigilance, aiming to systematically collect, assess, and analyse information about adverse events associated with the use of medications. Here are key elements involved in the monitoring of ADRs: (22)

Spontaneous Reporting Systems: Healthcare Professionals and Consumers: Encourage healthcare professionals and consumers to report suspected ADRs voluntarily to national pharmacovigilance systems or regulatory authorities.

Active Surveillance Systems: Database Surveillance: Utilize electronic health records, claims databases, and other healthcare databases to actively monitor and identify potential safety signals. Signal Detection Tools: Implement data mining techniques, statistical algorithms, and other tools to identify patterns and trends that may indicate potential ADRs.

Periodic Safety Update Reports: Regulatory Requirement: Prepare and submit PSURs to regulatory authorities at defined intervals, providing a comprehensive review of the safety profile of a drug. Updated Safety Information: Include information on new ADRs, changes in the frequency or severity of known ADRs, and any relevant risk minimization measures.

Risk Management Plans: Risk Identification and Mitigation: Develop RMPs to proactively identify, assess, and minimize risks associated with a drug.
Clinical Trials: Adverse Event Monitoring: Systematically collect and report adverse events during the conduct of clinical trials to assess the safety profile of investigational drugs.

Pharmacovigilance Agreements and Collaborations: International Collaboration: Engage in collaborations and information-sharing agreements between regulatory authorities, pharmaceutical companies, and international pharmacovigilance networks. Global Data Sharing: Share safety data globally to enhance the identification of ADRs and facilitate a coordinated response.

Literature Surveillance: Scientific Literature Review: Regularly review published scientific literature for new information on ADRs and safety concerns.
Integration with Pharmacovigilance Databases: Integrate findings from literature surveillance with data from pharmacovigilance databases for a comprehensive analysis.

Benefit-Risk Assessment: Regular Evaluation: Conduct regular benefit-risk assessments to evaluate the overall safety profile of medications in comparison to their therapeutic benefits. Decision-Making: Use benefit-risk assessments to inform regulatory decisions, labelling updates, and communication strategies.

Public Communication: Safety Alerts and Communication: Disseminate safety alerts and information to healthcare professionals and the public to enhance awareness of potential ADRs. Educational Initiatives: Develop educational materials to inform healthcare providers and patients about the importance of reporting and monitoring ADRs.

Serious Adverse Event:

A serious adverse event (SAE) in human drug trials are defined as any untoward medical occurrence that is caused at any dose

(a) Results in death

(b) Is life threatening

(c) Require in-patient hospitalization

(d) Prolongation of existing hospitalization

(e) Causes congenital anomaly/birth defect(23).

Research suggests that these events are often inadequately reported in publicly available reports(24).

Different regulatory agencies:

1. Drug Controller General of India (DCGI)
2. Central Drugs Standard Control Organization (CDSCO)
3. Indian Council of Medical Research (ICMR)
4. Ministry of Environment & Forests (MOEF)
5. Central Bureau of Narcotics (CBN)
6. Ministry of Health and Family Welfare (MHFW).(25)

Conclusion:

The result is that there is currently no widely accepted technique for ADR casualty evaluation. Pharmacovigliance is the science and spectrum of methods involved in detecting, evaluating, understanding, and preventing side effects or any other drug-related issue. The best way to understand adverse drug reactions, or ADRs, is through

There are other approaches, such as spontaneous reporting, careful observation, and database research.

After forty years, pharmacovigilance remains a vibrant area of clinical and scientific research. It is still essential to address the major challenges posed by the ever-increasing variety and potency of drugs, all of which carry an inevitable and sometimes unforeseen risk of harm. It is imperative to declare any negative consequences and toxins that.

REFERENCES:

1. www.pwc.com/pharma; drug-safety. Source: The Importance of Pharmacovigilance, WHO 2002.
2. World Health Organization. Safety of medicines. A guide to detecting and reporting adverse drug reactions – why health professionals need to take action. Geneva: World Health Organization; 2002.
3. Kumanan, R., Sudha, S., Vijayashre, P., Charumath, S., Gowridevi, K.C., Mahesh, M. „Imperative Approach on pharmacovigilance in Indian systems of medicines", International journal of pharma sciences and Research (ijpsr), 2010; 1(9): 378-390. 4. World Health Organization . Safety monitoring of medicinal products: guidelines for setting up and running a pharmacovigilance centre. Uppsala: Uppsala Monitoring Centre, World Health Organization; 2000.
5. Bord CA, Rachi CL; Adverse Drug Reactions in United States Hospitals. Pharmacotherapy, 2006; 26(5): 601-08.
6.Kumar, S.; Baldi, A. Pharmacovigilance in India: Perspectives and Prospects. Journal of Drug Delivery and Therapeutics2013, 3 (4), 237–246.
7. Shuka SS, Gidwani B, Pandey R, Rao SP, Singh V, Vyas A,Importance pharmacovigilance in Indian Pharmaceutical Industry, Asian Journal of Research in Pharmaceutical Science 2012; (2): 04-08.
8.Amarnath S, Jaikumar S, Basalingappa S, Thulasimani M,Ramaswamy S, Pharmacovigilance for Health Care Professional Students, Research Journal of Pharmaceutical,Biological and Chemical Sciences (RJPBCS)4 January-March 2013; 1204-1217.
9. Muraraiah S, Rajarathna K, Sreedhar D, Basavalingu D,Jayanthi C.R, A questionnaire study to assess the knowledge, attitude and practice of Pharmacovigilance in a paediatric tertiary care centre, Journal of Chemical and Pharmaceutical Research, 2011; 416-422. 10. Ghosh R, Bhatia M.S, Bhattacharya S.K, Pharmacovigilance: Master Key to Drug Safety Monitoring and its Status in India: Delhi Psychiatry Journal, 15 October 2012; 412-415. 11. Moore N. The role of the clinical pharmacologist in the management of ADRs. Drug Safety 2001; 24(1): 1-7.
12. Kulkarni RD. Reporting system for rare side effects of non-narcotic analgesics in India: Problems and opportunities. Med Toxicol 1986;1:110-3.
13. Protocol for National Pharmacovigilance Program. CDSCO, Ministry of Health and Family Welfare, Government of India. November, 2004.
14. Pharmacovigilance Programme for India (PvPI): Assuring Drug Safety. CDSCO, Directorate General of Health Services, Ministry of Health and Family Welfare. Available from: http://cdsco.nic.in/pharmacovigilance.htm.[Last accessed on 2013 August 20]. 15. Danan G, Benichou C, Causality assessment of adverse reactions to drugs- a novel method based on the conclusions of international consensus meetings: application to druginduced liver injuries, J ClinEpidemiol, 1993; 46(1):132-142.
16. Blanc S, Leuenberger P, Berger JP, Brooke EM, .Schelling JL, Judgments of trained observers on adverse drug reactions, ClinPharmacol Ther 1999; (25):493-498. 17. Bhosale U, Jaiswal S, Yegnanarayan R, Godbole G, A Pharmacovigilance Study of Anti Asthmatic Agents in Patients of Bronchial Asthma at a Tertiary Care Hospital, Journal of Clinical & Experimental Research,1May-August 2013; 26-30. 18. Sharma S, Phadnis P, Gajbhiye S, Pharmacovigilance: Its Awareness and Impact Care Teaching Medical

College in Central India Impact- Study in a Tertiary care Teaching Medical College in Central India, International Journal of Pharmaceutical Research and Bio- Science (IJPRBS), 2013; 2:234-247.
19. Padmavathi GV, Beere N, Divakara P, Suresh KP, Surendranath A, Patel RS, Screenplay of pharmacovigilance among nursing staff in Bangalore,2 February 2013; 365-370. 20. Leon L, Herbert A. Liberman, Joseph L. Kanig, Varghese Publishing House, Hind Rajasthan Building Dadar, Mumbai, 3rdEdition, 239-240.
21.Hall et al. 1995; Horbuckle et al. 1999; Tuntti and Neuroren 2002.
22.Moore N (2001). The role of clinical pharmacologist in management of ADRs. Drug safety, 211(1): 1-7.
23. The importance of pharmacovigilance; safety monitoring of medical products, Geneva, WHO, 2002.
24. J.P Loannidis, J Lau. Completeness of safety reporting in randomized trials: an evaluation of seven medical areas. JAMA, 2001; 285(4): 437-443.
25.Campbell, J. E.; Gossell-Williams, M.; Lee, M. G. A Review of Pharmacovigilance. West Indian Medical Journal2014, 63 (7), 771–774