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CONCEPT OF PHARMACOVIGILANCE

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ABSTRAT

The World Health Organization (WHO) (WHO, 2002) and Pal, Duncombe, Falzon, and Olsson (2013) define pharmacovigilance (PV) as the science and activity concerned with the detection, evaluation, understanding and prevention of adverse events. effects or any other drug-related problems. Pharmacovigilance plays an important role in the health care system through the monitoring and interaction of drugs and their effects in the body. The definition of pharmacovigilance, the objectives used in pharmacovigilance, and the types and components of pharmacovigilance were all summarised in this article. Constitution and goals of India's Pharmacovigilance Program (PvPI). An explanation of each National Adverse Drug Monitoring Center's (AMC) role Due to the fact that the pharmaceuticals are used in a manner that is not authorised by regulatory bodies, the biggest issue with this practise is the lack of methods for monitoring adverse drug reactions. Protection of the public's health is therefore not assured. Pharmacovigilance supports the safe and appropriate use of medicines. Spontaneous reporting of adverse drug reactions (ADRs) is an important component of pharmacovigilance. However, there is a significant under-reporting of ADRs. Adverse drug reactions have become a major problem in developing countries. Understanding pharmacovigilance could serve as the foundation for actions meant to increase reporting rates and lower ADRs. In India, a legitimate system for tracking adverse medication reactions was launched in 1986 with the help of 12 regional centres. India joined the World Health Organization's (WHO) Programme for International Drug Watching in 1997. This programme is run by the Upsala Monitoring Center in Sweden. Six regional centres were initially established in Mumbai, New Delhi, Kolkata, Lucknow, and for domestic ADR viewing, go to Chandigarh and Pondicherry. The Indian Pharmacopoeia Commission, which serves as the country's national coordination centre for the pharmacovigilance programme,

may prioritise promoting safe drug usage. 179 monitoring facilities for adverse drug reactions currently submit adverse occurrences to India's national coordination centre.

KEYWORDS: Pharmacovigilance, Adverse drug reactions (ADR), PvPI, new drugs and clinical trials, Pharmacology, DCGI, and the Indian programme.

INTRODCTION

According to the World Health Organization (WHO), pharmacovigilance (PV) as the pharmacological science and activities related to the monitoring, detection, evaluation, understanding and prevention of adverse drug reactions (ADRs) or any adverse drug reactions in the long and short term. Problems. The development of PV science was prompted by a variety of ADRs related to medication.[1-4] This led to the beginning of PV and the systematic study of ADR in medicine by WHO. Following this, a variety of ADRs were discovered, some of which are evident in (Table 1). ADR is considered to be the sixth most common cause of death. With over 6000 licenced manufacturers and more than 60000 branded formulations on the market, India, which has a population of 1.27 billion, is the fourth-largest producer of prescription pharmaceuticals in the world. ADRs account for 3-7% of hospital admissions in the United States. ADRs accounted for 1% of all hospital admissions in England between 1999 and 2008 as a whole. Side effects are also common in the Australian healthcare system and contribute to 1% of hospital admissions. Pharmacovigilance goes beyond spontaneous reporting and is more than just the assessment of marketed medicines. Pharmacovigilance goes beyond reviewing marketed drugs and includes more than just spontaneous reporting. By guaranteeing proper informed consent and institutional review boards (ethical committees), it has developed from a small aspect of drug control to a significant activity, and its scope has been broadened to include aid for patient safety during clinical trials; creating a safety profile for a new molecular entity and effectively informing various important stakeholders of that knowledge; establishment of a safety profile; selection of the first safe dose for usage in humans based on pharmacologic information gathered in animal research. This study links the expansion of pharmacovigilance to the evaluation of drug safety. Methods: The data from earlier published material was examined to obtain the ensuing information. The gathered data was assessed, collated, dissected, put back together, interpreted, and conclusions were drawn. Results: Gathering the information required to weigh the benefits and risks of medications is primarily a scientific endeavour. To ensure that information is acquired and used properly for the intended

purpose, good pharmacovigilance practises must be established. Pharmacovigilance has developed into a crucial component of drug control. By definition, determining the likelihood that a specific treatment is to blame for an observed adverse event is known as causation assessment.[1] It evaluates the connection between receiving drug therapy and experiencing an adverse event. It is a crucial part of pharmacovigilance, helping to improve the assessment of the risk-benefit ratios of medications.[2]

Pharmacovigilance is the science of monitoring the effects of drugs. PvPI, a pharmacovigilance program in India, is conducted by IPC and CDSCO. Both of these institutions are under the jurisdiction of the Ministry of Health and Family Welfare. PvPI is controlled by the IPC and the head program in DCGI. Manufacturers, drug importers, marketing. and is an essential part of evaluating ADR reports in early warning systems and for regulatory purposes.[3]

- **Concept of Pharmacovigilance**

- **What Pharmacovigilance**

Pharmakon (Greek) = Medicinal substance

(Latin) Vigila = to watch

DEFINITION

- **Definition of Pharmacovigilance**

According to the (WHO) Pharmacovigilance is the science and actions concerned with the identification, evaluation, comprehension, and avoidance of unfavourable effects of drugs that are currently on the market or being tested.

The task of maintaining a robust pharmacovigilance system to track adverse drug reactions during drug development and later, when the pharmaceuticals are released, falls to the drug regulatory bodies.

Fig. 1: Pharmacovigilance Services.

- **Objectives of Pharmacovigilance**

Objective

- An essential factor to consider is how to improve patient care and safety when using medications in conjunction with medical and non-medical therapies.
- The primary goals of pharmacovigilance include demonstrating the efficacy of medications by tracking their adverse effect profile over a long period of time from the lab to the pharmacy; keeping track of any severe side effects of medications; enhancing public health and safety in relation to medication use; encouraging the safe, prudent, and economical use of medications; promoting understanding, education, and clinical training in pharmacovigilance; and effectively communicating with the generic pharmaceutical industry.[6]
- The goals of pharmacovigilance studies also include educating patients, doctors, and practitioners on the proper use of medications, as well as developing protocols and procedures for gathering and analysing their data.[6,7]

➢ **Type and components of Pharmacovigilance**

There are four important types in Pharmacovigilance such as

1. **Passive surveillance**

- Spontaneous Reports
- Case Series

2. **Stimulated Reporting**

3. **Active surveillance**

- Sentinel sites
- Drug event monitoring
- Registries

4. **Cohort event monitoring**

5. **Comparative observational study**

- **Cross-sectional study (survey)**
- **Case- control study**

6. **Targeted clinical investigations**

7. **Descriptive studies**

- Natural history of disease
- Drug utilization study

1. **Passive surveillance**

- The use of spontaneous adverse event reports voluntarily reported to the marketing authorization holder or regulatory is a component of passive surveillance strategies. Here, information about the negative reaction is gathered and stored in a national or local database. Although the reporter's name is kept secret, the reporting forms can be used to retrieve patient-related information such as country, age, gender, and co-morbidities that already existed.

Fig. 2: Pharmacovigilance Passive surveillance.

Examples of spontaneous reporting systems including the

1. The FDA-run FAERS (FDA Adverse Event Reporting System) database
2. The WHO Global Individual Case Safety Report (ICSR) database, called VigiBaseTH
3. Eudra Vigilance Medicines Agency for Europe
4. India currently lacks any dedicated systems for spontaneous reporting. (Selected qualifying medical schools, facilities, and hospitals have been authorised to serve as ADR Monitoring Centers. They gather the Individual Case Safety Reports (ICSRs), examine them, and submit their findings to the appropriate regulatory body. An additional approved person for the collection of ICSRs, as well as for its follow-up and online database entry in Vigi-Flow software, is the technical associate from the Department of Medical Sciences at Banaras Hindu University.[4]

➢ **Spontaneous reports**

1. Regionalization
2. Taking back additional data
3. Having access to the necessary pre- and post-marketing data
4. Facts on drug use in detail.
5. Standardised assessment of importance and causation

- A report of one or more adverse drug reactions in a patient who received the drug, made to a firm or regulatory authority by a customer or healthcare practitioner.
- Has a significant impact on identifying safety signals after the medicine is introduced.
- Issue warnings for uncommon adverse events (AEs) that weren't seen in prior clinical trials or according to marketing research
- Offers crucial details on at-risk populations, risk factors, and clinical traits of well-known

severe adverse medication reactions.

- Doctors and other healthcare professionals are given forms to complete for potential ADR information; once completed, they are required to notify the drug regulatory authorities. (For instance, TGA (Therapeutic and Goods Administration) for Australia, DCGI for India, and USFDA for the United States of America)[5]

➢ **Case Series**

- A series of case reports can show that a drug and adverse events are related.
- Usually more beneficial for generating hypotheses than for conclusively proving a
- connection between drug exposure and result
- Specific adverse reactions, such as anaphylaxis, aplastic anaemia, toxic epidermal necrolysis, and Stevens-Johnson syndrome, are more common with medication therapy and are voluntarily reported for thorough and prompt follow-up.

2. Stimulated Reporting

- A technique for encouraging and facilitating health professionals' reporting of new products or limited-time uses.
- Methods: Systematic encouragement of AE reporting and online AE reporting

- DISADVANTAGE
- Data are frequently unfinished.
- It is useless to calculate precise incidence rates.

3. Active Surveillance

- This method strives to count the number of adverse drug reactions totally through a pre-planned process and aims to monitor a specific set of medication-related adverse events. It is often referred to as safety monitoring or toxicity monitoring.
- To fully determine the number of AE through an ongoing, pre-planned approach. For instance: Monitoring patients who have taken a specific medication.
- Easier to obtain thorough information on specific AE reports.

➢ **Sentinel sites**

- Active surveillance can be achieved by reviewing medical records or interviewing patients and/or physicians in a sample of sentinel sites to obtain complete and accurate data on adverse events reported at these sites.

- Selected sites may provide information such as data on specific patient subgroups that would not be available in a passive spontaneous reporting system.
- **Weakness**

Bias in selection

Few patients

Cost increases

- This specific approach is more effective for medications used primarily in institutional settings, such as hospitals, nursing homes, hemodialysis centres, etc. that can offer an infrastructure for specialised reporting.

➢ **Drug Event Monitoring**

- A follow-up questionnaire can be emailed to each doctor or patient at predetermined intervals.
- Patients are identified by electronic prescription data or automated health insurance claims.
- The questionnaire can include data on the patient's demographics, therapeutic indication, length of therapy (including start dates), dosage, clinical events, and reasons for discontinuation.
- Restrictions: Inadequate physician and patient response rates and the scattershot nature of data collection can mask critical signals.
- Cohort Event Monitoring (CEM), a proactive pharmacovigilance technique supported by the World Health Organization and other organisations, is a variation of Drug Event Monitoring.
- Patients are initially identified in this system using electronic prescription data or automatically generated health insurance claims.
- To acquire outcome data, a follow-up questionnaire can then be sent to each prescribing doctor or patient at predetermined intervals.
- The questionnaire can include pertinent data, such as demographics, therapeutic indication, length of therapy, dosage, clinical events, and reasons for therapy cessation.[8]

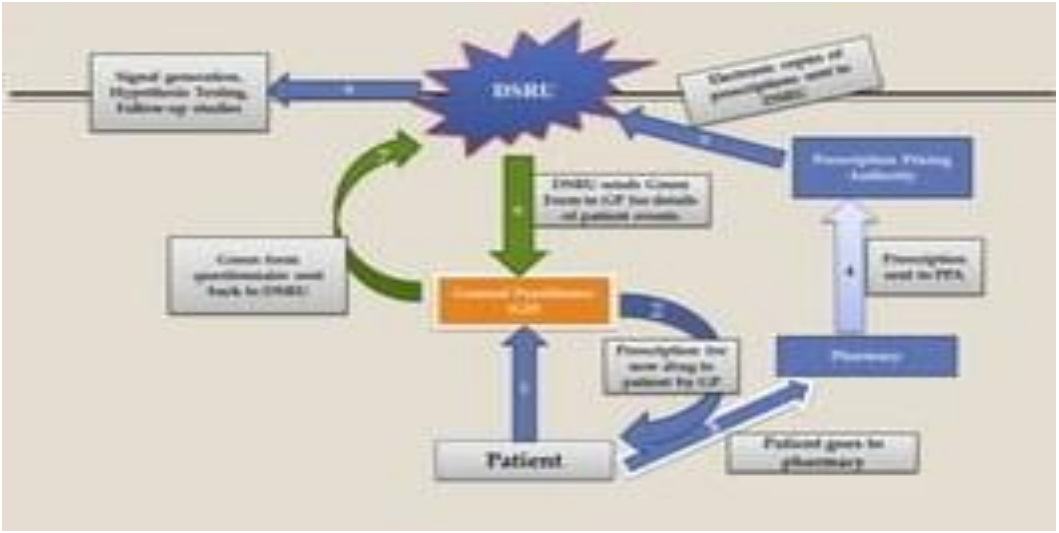

Fig. 3: Drug Event Monitoring.

➢ **Registries**

- A registry is a collection of patients who arrive with similar symptoms. Registries for diseases or pregnancy, for instance.
- Vary based on the patient's condition.
- A common questionnaire can be used to gather information.

➢ **Strengths**

- Studies with a single cohort can calculate incidence.
- Helpful for signal amplification of uncommon results.
- Investigating the safety of an orphan medication prescribed for a particular condition

4. Cohort Event Monitoring

- With this approach, the surveillance study is planned before the pharmaceutical therapy ever starts. A group of individuals is exposed to a drug for a predetermined amount of time and is closely monitored throughout treatment.
- Monitoring is done for adverse drug reactions or those related to one or more medications taken along with the target drug.

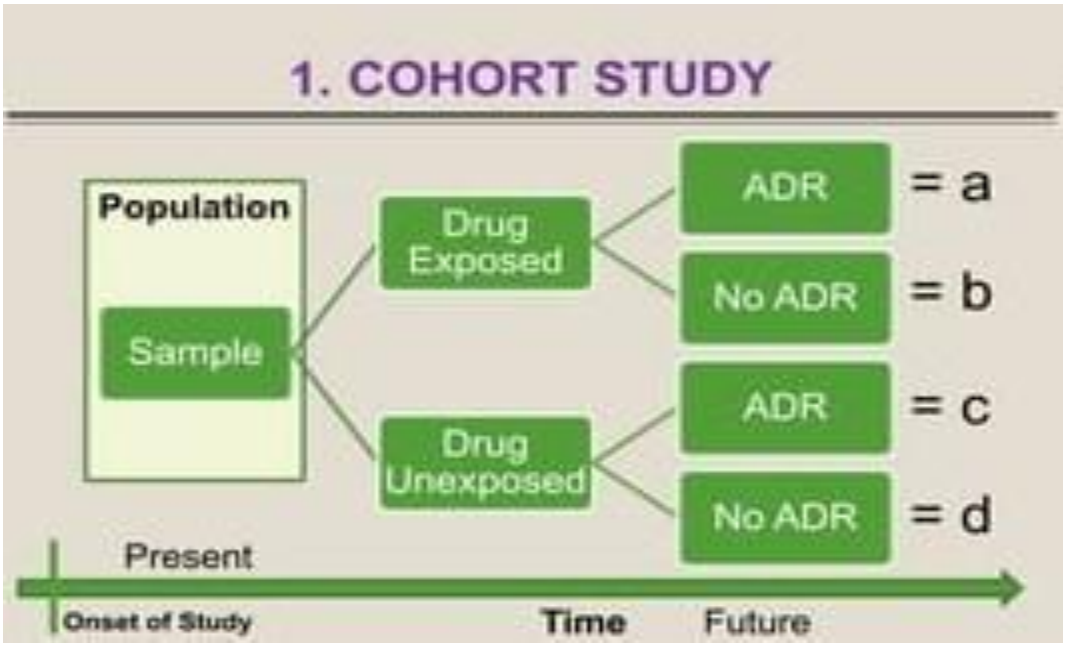

Fig 4: Cohort Study.

5. Comparative Observational Studies

- Traditional epidemiologic methods are a key component in the evaluation of adverse events.
- Observational study designs are useful in validating signals from spontaneous reports or case series.

Types of designs

(i) Cross-Sectional studies

(ii) Case-Control studies

(i) Cross-Sectional Studies

- Information gathered from a group of patients at one particular moment (or period), irrespective of exposure or disease status.
- mostly used to collect information for surveys or ecological analyses
- Significant drawback: It is impossible to directly link exposure to results.
- Advanced: When data or serial time points can be gathered, it is best used to evaluate trends over time or the prevalence of a disease at one particular time point.

(ii) Case-Control study

- Patients chosen from the source population as controls are those without the disease or relevant occurrence.

- It is important to choose the controls since their exposure status prevalence mirrors that of the source population's.
- The odds ratio is then used to compare the exposure status of the two groups.

- **Advantages**

✓ Easy to complete, quick,

✓ reasonably priced

✓ Few subjects are actually needed, and they are appropriate for rare disorders.

- **Disadvantage**

✓ Problem with Bise

✓ It may be challenging to choose an adequate control group.

✓ Tt is unclear how time is related.

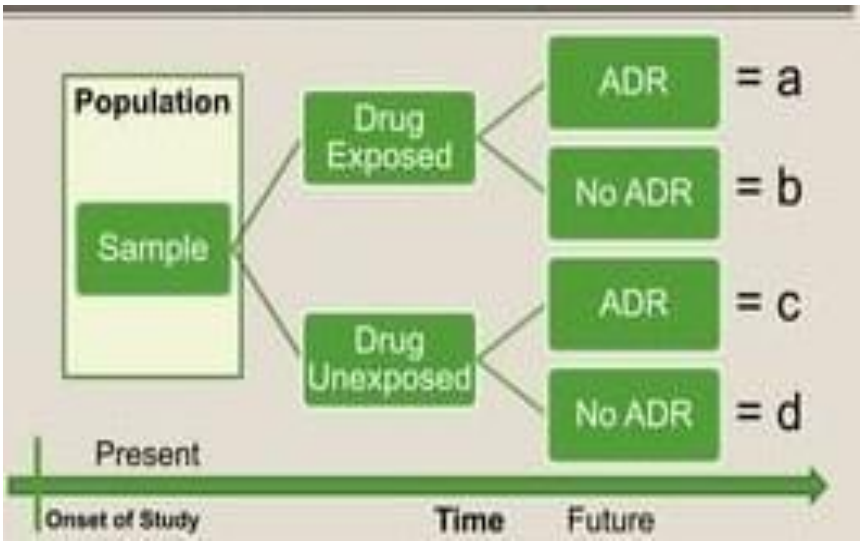

Fig. 5: Case Control studies.

6. Targeted Clinical Investigations

- These studies are carried out to discover and characterise the negative effects of a medicine in particular populations, such as elderly individuals, pregnant women, and persons with certain genetic diseases.
- Additional clinical studies may be required to assess the mechanism of action for ADRs if high risk is found in pre-approval clinical trials.
- In rare cases, pharmacodynamic and pharmacokinetic studies may be carried out to ascertain whether a specific dose can raise the risk of adverse effects in patients.
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ascertain whether a specific dose can raise the risk of adverse effects in patients.

- The group of patients who are more likely to experience negative reactions can be identified via genetic testing.
- It may also be necessary to conduct specific research to look into potential drug-drug and food-drug interactions.
- Research may include medication concentration monitoring in patients and healthy volunteers as well as population pharmacokinetic studies.
- The elderly, kids, and people with renal or hepatic disorders may be among the population.
- The extent of the danger (or benefit) in such populations may be determined and quantified using further analysis.

7. Descriptive studies

- Mainly used to determine the prevalence of drug use in a given population and/or to measure the background rate of outcome events.

1. Natural history of disease: concentrated on the natural history of disease, including the characteristics of ill patients and the distribution of disease in particular populations, as well as measuring the incidence and prevalence of potentially interesting consequences.

2. Drug utilization study: These studies offer information on particular groups, such as the elderly, kids, or people with liver failure, and are frequently stratified by age, gender, concurrent medications, and other factors.[8]

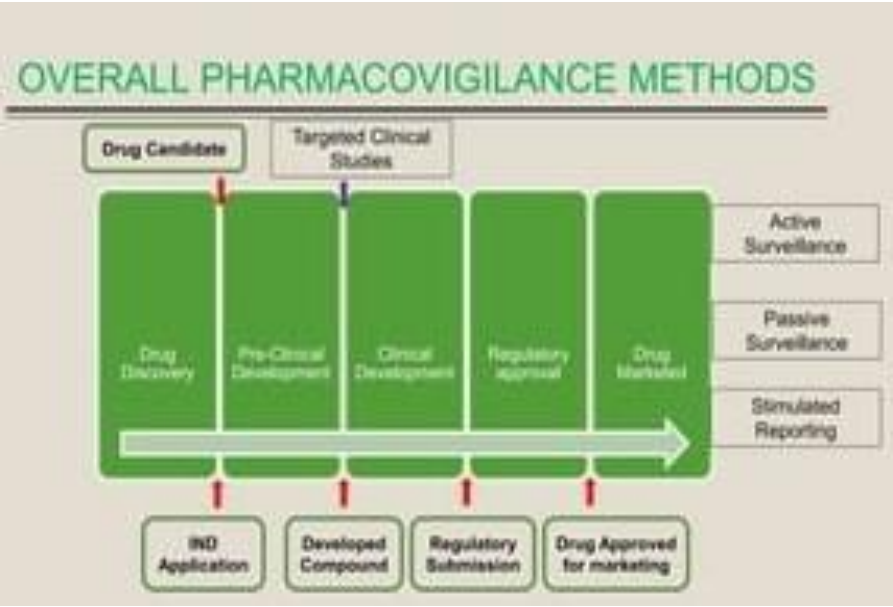

Fig. 6: Overall Pharmacovigilance.

❖ **Component of Pharmacovigilance**

- **Pharmacovigilance operating models must focus on four key components to become proactive, resource efficient, and business aligned**

1. Core Capabilities

Pharmacovigilance provides pharmaceutical companies with four main opportunities:

- Case management of adverse occurrences, including expedited reporting;
- Summary reporting;
- Risk management; and
- Signal intelligence.

2. Strategy

The benefit-risk aspects of each product must be considered in business planning. Pharmacovigilance, when used successfully, can create a competitive advantage by creating a strong benefit-risk profile and improving patient identification.

3. Global Networks

Pharmacovigilance (PV) needs to be governed by a variety of regulatory frameworks that are tailored to various markets. To preserve visibility and consistency and enable local responsiveness, a network of centralised and local capabilities is needed.

4. GOVERNANCE

Clear governance is necessary for the effective escalation and settlement of issues. While preserving compliance, a closed loop method that is closely connected to the organization's overall crisis management process can reduce safety hazards.[8,9]

❖ **Constitution And Objectives Of Pharmacovigilance Program Of India (PvPI)**

• India's pharmacovigilance

1. CSCA, Central Drug Standard Control Association

- Ministry of Health and Family Welfare, DGHS

2. PV in India: Legislative Requirements

- The Drug and Cosmetic Act of 1945, Schedule Y

• India's Pharmacovigilance Program

A nationwide Pharmacovigilance Program is being launched by the Centre Drugs Standard Control Organization (CDSCO), Directorate General of Health Service, under the auspices of the Ministry of Health and Family Welfare, Government of India, in collaboration with the India Pharmacopoeia Commission, Ghaziabad. The program's goal is to safeguard patient health by ensuring the safety of their medications. The Indian Pharmacopoeia Commission, Ghaziabad will serve as the program's National Co-ordinating Center (NCC). A Steering Committee will be in charge of managing the Center's operations.

The Government of India launched the Pharmacovigilance Program of India (PvPI) on July 14, 2010, with the All-India Coordination Centre for monitoring Adverse Drug Reactions (ADR) in the nation for self-directing Public Health. 22 ADR Monitoring Centers, including AIIMS in New Delhi, were established as part of the programme this year (2010). The National Coordination Center was relocated from the All-India Pharmacopeia Commission in Ghaziabad, Uttar Pradesh, on April 15, 2011, to ensure a more effective implementation of this initiative.[8]

Additionally, the controlled circumstances under which drugs are tested in clinical trials do not always correspond to how they would be used in actual life. A medication must have predictable benefits that outweigh any potential for negative side effects in order to be deemed safe. Therefore, to obtain a comprehensive safety profile of the drug. Pharmacovigilance, or ongoing post-marketing surveillance, is crucial. Pharmacovigilance uses data from any source to assess the safety of medications. These include mechanisms for reporting accidental drug reactions (ADRs), updated medical literature from throughout the world, actions taken by regulatory bodies abroad, etc.[12,13]

PvPI's main objective is to gather data, process it, and analyse it before using the conclusions to suggest regulatory responses and inform the public and the medical community about the hazards.[9]

❖ **Objective Governance structure of the Pharmacovigilance Programme of India (PvPI)**

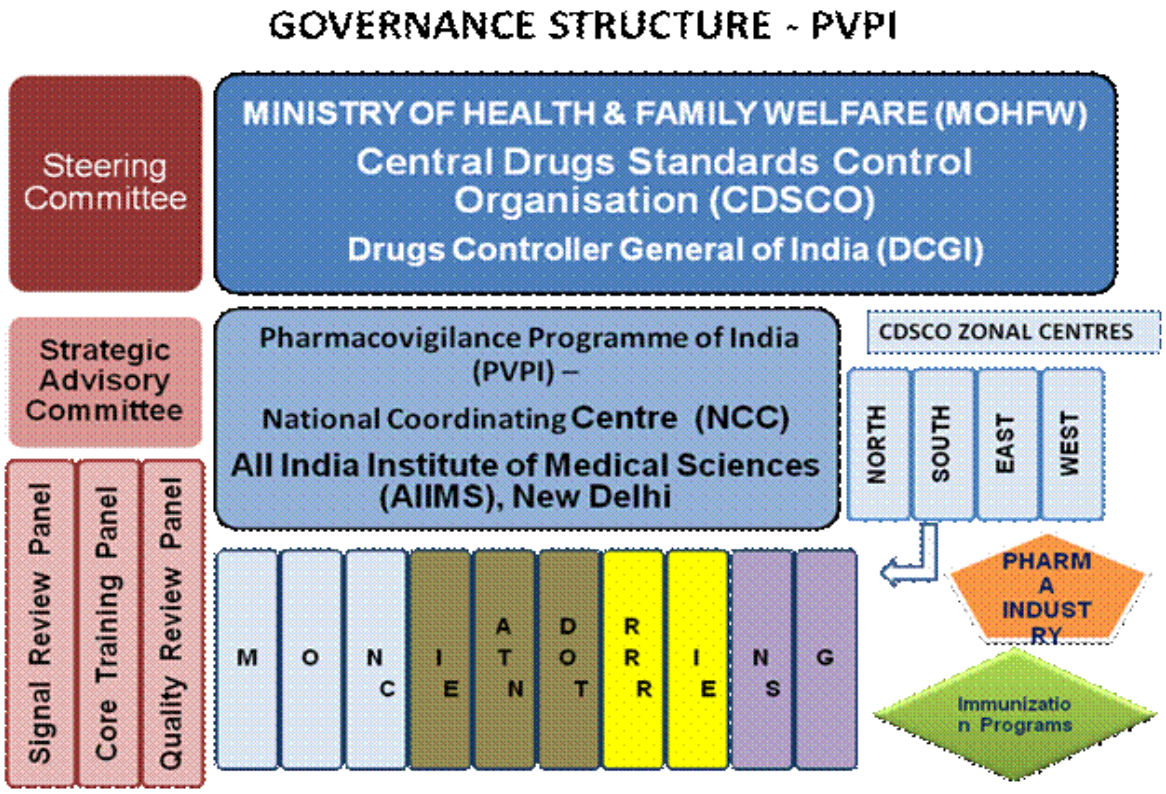

Fig. 7: Governance structure.

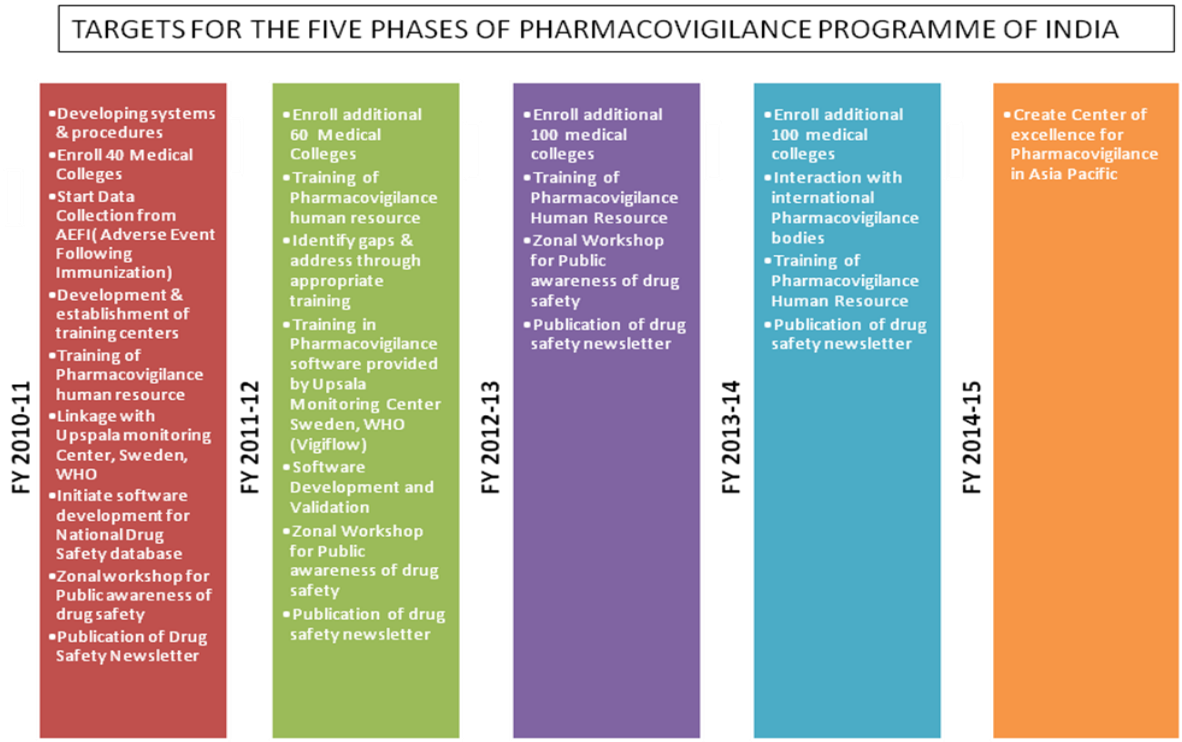

Fig. 9: Targets of Pharmacovigilance Programme of India.

Objective

1. To keep track of adverse drug reactions (ADR) among Indians
2. To establish a national mechanism for reporting patient safety
3. To locate and evaluate the new signal ADR from the cases that have been reported
4. To evaluate the benefit-risk balance of commercially available drugs
5. To produce evidence-based information on the medicine's safety
6. To assist regulatory bodies in making decisions about the use of pharmaceuticals
7. To minimise danger, it is important to share information about how to use medications safely with all relevant parties.
8. Become a leading national hub for Pharmacovigilance activities
9. Communicate at the same level as international requirements for medication safety monitoring.[8]

❖ **List of ADR Monitoring Centres Under Pharmacovigilance Programme of India (PVPI)**

Sr. NO.	Address	Coordinators	Email Address

National Coordinating Centre (NCC)

1	All India Institute of Medical Sciences, Department of Pharmacology, New Delhi	Dr. Y.K. GuptaNation Coordinator	yk.ykgupta@gmail.com, pvpi.ncc@gamil.com

ADR Monitoring Centres (AMC)

1	Department of Pharmacology, Therapeutics and Toxicology, Govt. Medical College, BakshiNagar, Jammu.	Dr. Vishal Tandon	Dr.vishaltandon@yahoo.com
2	Department of Pharmacology, PGIMER, Chandigarh	Dr.Bikash Medhi	Dr.bikashus@yahoo.com
3	Department of Pharmacology, R. G. Kar Medical College,Kolkata	Dr. Anjan Adhikari	Adr.rgk.pharma@gmail.com
4	Department Of Pharmacology, Lady Harding Medical College, New Delhi	Dr. H. S. Rehan	harmeetrehan@hotmail.com
5	Department of ClinicalPharmacology, Seth GS Medical College and KEM Hospital, Parel, Mumbai	Dr. Urmila Thatte	pvpiitakem@gamil.com
6	School of Tropical Medicine, Department of Clinical and Experimental Pharmacology, Chittaranjan Avenue, Kolkata	Dr. Santanu Tripathi	Stm.pvpi@gmail.com
7	Pharmacy Department, JIPMER,	Dr. C Adithan	adithan18@gmail.com

	Pondicherry		
8	Clinical Pharmacy Division, JSS Medical College Hospital, Karnataka	Dr. Parthasarathi G	partha18@gmail.com
9	Guwahathi Assam Medical College's Pharmacology Department	Dr. Maneala Lahkar	drmlahkar@rediffmail.com
10	Madras Medical College's Institute of Pharmacology is in Chennai.	Dr. R Nandini	Pvpi.chennai@gmail.com
11	Indore-SAIMS Ujjain's Medical College's Department of Pharmacology	Dr. Chhaya Goyal	Chhayal@gmail.com
12	Kanpur, Uttar Pradesh's GSVM Medical College, Swaroop Nagar, has a department of pharmacology.	Dr. SP Singh	singhdrsp@gmail.com
13	Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences, Department of Pharmacology, Rohtak, Haryana.	Dr. MC Gupta	drmcgupta@yahoo.com dr.mcgupta57@gmail.com
14	Dayanand Medical College and Hospital, Department of Pharmacology, Ludhiana, Punjab	Dr. Sandeep Kaushal	Skaushal1@yahoo.com
15	Sher-i-Kashmir Institute of Medical Sciences, Department of Clinical Pharmacology, Srinagar, J. and K.	Dr. ZA Wafai	drzawafai@gmail.com
16	Dehradun, Uttarakhand's Himalayan Institute of Medical Sciences	Dr DC Dhasmana	dhasmanadc@gmail.com
17	Santosh Medical University's Department of Pharmacology is located in Santosh Nagar, Ghaziabad.	Dr. VC Chopra	Vipen.chopra@gmail.com
18	SMS Medical College's Pharmacology Department is located in Jaipur.	Dr. Mukul Mathur	Mathurmukul@rediffmail.com Coordpvpimsjp@rediffmail.com
19	Christian Medical College's Clinical Pharmacology Department is located in Vellore, Tamil Nadu.	Dr. Sujith Chandy	sjcgandy@gmail.com

❖ **Function of the stakeholders in the Programme**

▪ **Functions of the Stakeholder**

1) PvPI ADR Monitoring Centre in Medical College (PvPI) (AMCs)

- Gathering ADR reports
- Follow up with the complainant to ensure compliance with SOPs
- Adding data to Vigiflow
- Using Vigiflow to report to the PvPI National Coordinating Center (PvPI NCC) and
- Attaching the original source data for each ADR case.
- Educating, enlightening, and providing feedback to doctors through newsletters
- Spread by PvPI NCC

2) PVPI ADR Monitoring Centers outside of medical schools Corporate hospitals, independent institutes, the pharmaceutical industry, and public health initiatives

- Gathering ADR reports
- Follow up with the complainant to ensure compliance with SOPs
- Report the information to CDSCO HQ.

3) National Coordinating Center for PVPI (PvPI NCC, IPC Ghaziabad)

- Creation of SOPs, instructions, and training manuals
- Data gathering Verify for completeness again. Causality Evaluation, etc.
- Hold workshops for training for all registered centres.
- Publishing a newsletter on medication safety
- Examination of the PMS, PSUR, and AEFI data that CDSCO HQ provided

4) CDSCO Zonal/Subzonal Offices

- Report to the CDSCO HO.
- Offer ADR monitoring centres financial, administrative, and purchasing help[8]

5) CDSCO, HQ New Delhi

- At IPC Ghaziabad, implement the necessary regulatory decisions and actions based on the recommendations of PVPI NCC.
- Gathering ADR[9]

CONCLUTION

If every member of the healthcare industry, including doctors, nurses, pharmacists, and others like patients, reports all ADRs, the regulatory body can act quickly and potentially prevent the availability of illegal drugs in India. Systems for pharmacovigilance are required to protect the public's health. Information creation that can support healthcare processes has received only minor significance. One of the main responsibilities of pharmacovigilance is the gathering and dissemination of this data.

The ability to identify which people are at risk from drug use is a requirement for pharmacovigilance types. The objective of India's pharmacovigilance programme, also known as adverse drug reaction observation and reporting programmes, is to detect the dangers associated with the use of medications. If medications are to be used responsibly, a Pharmacovigilance system that is properly functional is essential. Monitoring medications for

risk will be beneficial for medical practitioners, regulatory bodies, pharmaceutical businesses, and customers.

REFERENCES

1. World Health Organiation(WHO), Uppsala Monitoring Centre(internet). The use of WHO-UMC system for standard case causality assessment available at http://www.whoumc.org/graphics/4409.pdf.
2. Macedo AF, Marques FB, Ribeiro CF, Texeira F. Causality assessment of adverse drug reactions: comparision of the results obtsined from published decisional algorithms and from the evaluations of an expert panel. Pharmacoepidemiological drug sof., 2005; 14: 885-890.
3. Arimone Y, Begnad B, Miremont, Salame G, Fourrier-Regalt A, Moore N, Molimard M et al, agreement of expert judgment in causality assessment of adverse drug reactions. Eur J Clin pharmacology, 2005; 61: 169-173.
4. S.K. Gupta. Textbook of Pharmacovigilance. 2nd Edition. Jaypee Brothers Medical Publishers.2019.
5. Elizabeth B. Andrews, Nicholas Moore. Mann's Pharmacovigilance Edition. Wiley Blackwell, 2014.
6. WHO, Pharmacovigilance: ensuring the safe use of medicines, Geneva: WHO 2004
7. Livio F, Renard D, Buclin T. Pharmacovigilance. Rev Med Suisse 2012;8:116-9
8. Alwhaibi, M., & Al Aloola, N. A. (2020). Healthcare students' knowledge, attitude and perceptionof pharmacovigilance: A systematic review. *PloS one*, *15*(5),e0233393
9. Lihite, R. J., & Lahkar, M. (2015). An update on the Pharmacovigilance Programme of India. Frontiersin pharmacology, 6, 194.
10. Pharmacovigilance guidance document, Indian of Pharmacopeia commission and CDSCO.
11. Kalaiselvan V. Prakash J, Singh GN. Pharmacovigilance programme of India. Frontiers in Pharmacology, 2015.
12. S.K. Gupta. Textbook of Pharmacovigilance. 2nd Edition. Jaypee Brothers Medical Publishers, 2019.
13. Ankur Rohilla, Nishant Singh, Vipin Kumar, Mohit Kumar Sharma, Amarjeet Dahiya, Ashok Kushnoor; Pharmacovigilance: Needs and Objectives, J. Adv.Pharm.Edu. & Res. 2012: 4: 201- 205.
14. Kalaiselvan, V., Srivastava, S., Singh, A., & Gupta, S. K.(2019). Pharmacovigilance in

India: Present Scenario and Future Challenges. *Drug safety*, *42*(3): 339–346.