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A REVIEW ON PHARMACOVIGILANCE PROGRAMME OF INDIA

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Abstract:

In India, a proper adverse drug reaction monitoring system was started in 1986 with 12 regional centres. In 1997, India became the member of World health organization Programme for International Drug watching managed by the Upsala Monitoring Centre, Sweden. At origination, 6 regional centres were created in Mumbai, New Delhi, Kolkata, Lucknow, Pondicherry, and Chandigarh for ADR watching within the country. Promoting safe use of drugs may be a priority of Indian Pharmacopoeia Commission that functions as the National Coordination Centre for Pharmacovigilance Programme of India. There are 701 Adverse Drug Reactions Monitoring Centres presently report adverse events to National coordinative centre in India.

Keywords: *Adverse drug reaction, AMC, Pharmacovigilance*

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INTRODUCTION:

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects of a drug or any other possible drug-related problems. The concept of pharmacovigilance or monitoring of drug safety dates back to much before 150 years, however, findings published in 1893 in The Lancet confirmed for the first time the establishment of a reporting system for suspected adverse drug reactions (ADRs).

Pharmacovigilance, a French word, was described as "a discipline involving detection, evaluation and prevention of undesirable effects of medicines." This was derived from the Greek "pharmakon" meaning a drug or medicine and from the Latin "vigilans" meaning watchful or careful. World Health Organization (WHO) defines pharmacovigilance as "the science and activities related to the detection, assessment, understanding and prevention of adverse effects or any other drug related problem.

History of pharmacovigilance:

The history of Pharmacovigilance started 169 years ago, on Jan 29, 1848, when a young girl (Hannah Greener) from the north of England died after receiving chloroform anesthetic before removal of an infected toenail. Sir James Simpson had discovered that chloroform was a safer and powerful anesthetic, and he had introduced it in clinical practice. The causes of Hannah's death was investigated to understand what happened to Hannah, but it was impossible to identify what killed her. Probably she died of a lethal arrhythmia or pulmonary aspiration

As a result of other deaths and alerts raised by the clinicians and the public about the safety of anesthesia, The Lancet Journal established a commission to take on this problem. The commission exhorted English doctors, including the doctor in colonies, to report deaths caused by the anesthesia. The results were published in The Lancet in 1893 .

The US Federal Food and Drug Act was formed on June 30, 1906, and it established that drugs must be pure and free of any contamination. Furthermore, in 1911, this organization forbade false therapeutic indications of drugs . In 1937, there were 107 deaths in the USA, because of the use of sulfanilamide elixir, containing diethyl glycol as the solvent. This solvent was considered the cause of deaths, but the manufactory companies were not aware about its toxicity at that time . Consequently, the Federal Food, Drug and Cosmetic Act was established in 1938; its aim was to renovate the public health system. In 1938, Douthwaite supposed that acetylsalicylic acid (ASA) could cause melena . The study of the gastrointestinal toxicity of ASA showed different outcomes. However, in 1955, it was proved that ASA can cause gastrointestinal diseases and therefore it is currently contraindicated in patients with gastrointestinal ulcers .

In 1961, a big change of European Pharmacovigilance happened following the tragedy of Thalidomide. Dr. McBride, an Australian doctor, wrote a letter to the editor of the Lancet Journal, in which he suggested a connection between congenital malformation of babies and thalidomide. In fact, he observed that the incidence of congenital malformations of babies (1.5%) had increased up to 20% in women who had taken thalidomide during pregnancy . At the same time, during a Pediatric Convention in Germany Dr. Lenz suggested a correlation between malformations and thalidomide and his suspect was published in a German Journal. In 1973, a retrospective study showed the correlation between the congenital malformations of babies and the ingestion of thalidomide during pregnancy .

In 1964, the "Yellow card" (YC) was structured in the UK. YC is a specific form to compile a spontaneous report of drug toxicity . In USA (1962), the amendment, requiring safety and efficacy data of drugs before premarketing submission, was approved.. In Europe (1965), the disaster of thalidomide stimulated the development of a European legislation with the EC Directive 65/65 . In 1966, a pilot study of Boston Collaborative Drug Surveillance Program started. In 1968, the WHO Programme for International Drug Monitoring was instituted and ten members participated in this program (Australia, UK, USA, Germany, Canada, Ireland, Sweden, Denmark, New Zealand, and Netherlands). Italy participated in this program in 1975 . Many studies of observed adverse drug reactions were conducted between 1968 and 1982 . In 1992, the European Society of Pharmacovigilance (ESoP) was funded, turned into the International Society of Pharmacovigilance (IsoP). The aims of this society were to promote Pharmacovigilance, and enhance all aspects of the safe and proper use of medicines . In 1995, the European Medicines Agency (EMA) was set up . In 2001, EudraVigilance was funded. It is the official European database for managing and analyzing information on suspected adverse reactions to medicines which have been authorized for the market or being studied in European clinical trials . A major change in European Pharmacovigilance was observed with the new legislation (Directive 2010/84/EU), in 2012 .

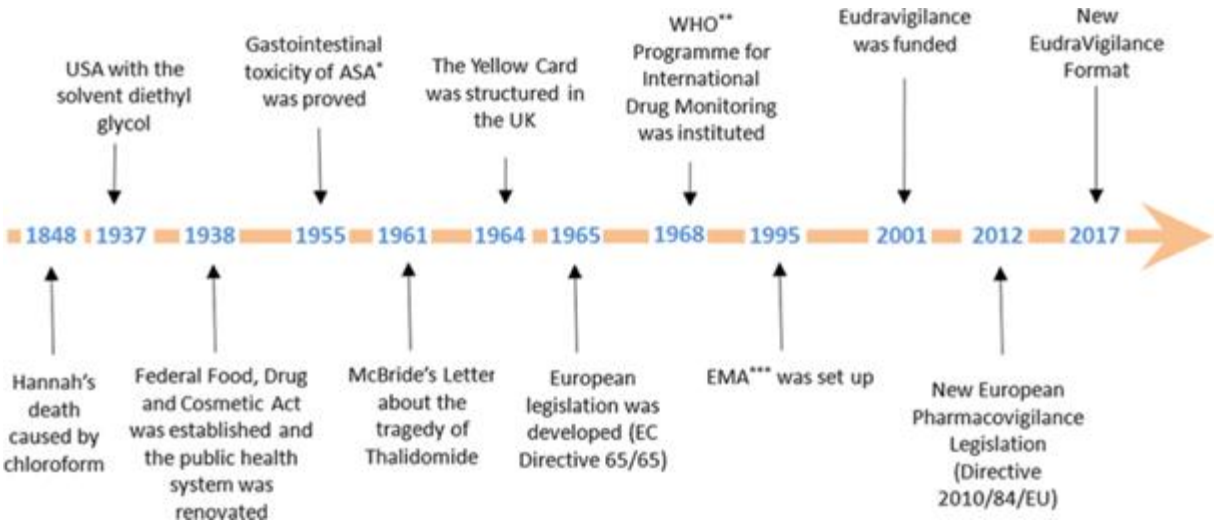

Fig no 1: History of Pharmacovigilance

NEED OF PHARMACOVIGILANCE:

Today, the need for an efficient pharmacovigilance system has been realized more than ever to ensure safe use of drugs. There are multiple reasons for this increasing necessity of pharmacovigilance. Some of these are as follows:

1.Unreliability of pre-clinical safety data

- Well-controlled conditions
- Small and specific sample size
- Pressure from various groups to reduce time to approval.

2.Changing pharmaceutical marketing strategies

- Aggressive marketing
- Direct advertising to consumer
- Launch in many countries at a time.

3.Changing physician's and patient's preferences

- Increasing use of newer drugs
- Increasing use of drugs to improve quality of life
- Shift of supervised to self-administered therapy.

4. Easy accessibility

- Increasing conversion of prescription drugs to over the counter drugs
- Easy access to drug information on the Internet
- Easy availability of complementary medicines
- Easy availability of substandard drugs.

PHARMACOVIGILANCE PROGRAMME OF INDIA(PvPI):

Pharmacovigilance programme of India was operationalized in July 2010 by Ministry of Health and Family Welfare (MoHFW), Government of India with a mission to reduce the risks associated with the use of medicines in Indian population. The AIMS, New Delhi was established as National Coordinating Centre for PvPI. Later on, Ministry of Health and Family Welfare (MoHFW), Government of India on 15th April 2011, recasted this programme and shifted the National Coordination Centre from AIIMS, New Delhi to Indian Pharmacopoeia Commission(IPC) Ghaziabad.

Before registration and marketing of medicine in the country, its safety and efficacy experience is based chiefly on the use of the medicine in clinical trials. These trials primarily detect common adverse reactions. Some important reactions, such as those, which take a long time to develop, or those, which occur rarely, may not be detected in clinical trials. In addition, the controlled conditions under which medicines are used in clinical trials do not necessarily reflect the way they will be used in practice. For a medicine to be considered safe, its predictable benefits should be greater than any associated risks of harmful reactions. So, in order to gain a complete safety profile of medicine, a continuous post-marketing monitoring system i.e. pharmacovigilance is essential. In order to screen the safety of medicine, information from many sources is used for pharmacovigilance. These include spontaneous (ADRs) reporting mechanism; medical literature published worldwide, action taken by regulatory authorities in other countries, etc. Meanwhile there

exist considerable social and economic consequences of adverse drug reactions and the positive benefit/cost ratio of employing appropriate risk management (there is a need to engage healthcare professionals and the public at large, in a well-structured programme to build synergies for monitoring adverse drug reactions in the country). The purpose of the PvPI is to collate data, process and analyze it and use the inferences to recommend regulatory interventions, besides communicating risks to healthcare professionals and the public.

MISSION:
Safeguard the health of the Indian population by ensuring that the benefits of use of medicine outweigh the risks associated with its use.

VISION:
To improve patient safety and welfare in Indian population by monitoring the drug safety and thereby reducing the risk associated with use of medicines.

OBJECTIVES:

- To create a nation-wide system for patient safety reporting
- To identify and analyze the new signal (ADR) from the reported cases
- To analyses the benefit - risk ratio of marketed medications
- To generate the evidence based information on safety of medicines
- To support regulatory agencies in the decision making process on use of medications
- To communicate the safety information on use of medicines to various stakeholders to minimize the risk
- To emerge as a national center of excellence for pharmacovigilance activities
- To collaborate with other national centers for the exchange of information and data management
- To provide training and consultancy support to other national pharmacovigilance centers located across globe

IMPLEMENTATION OF PVPI:
IPC assumed the need for establishing local hospital based centers across the nation for the better patient safety. It was significant to monitor both the known and previously unknown side effects of medicines in order to determine any new information available in relation to their safety profile. In an enormous country like India with a population of over 1.2 billion and with vast ethnic variability, different disease prevalence patterns, practice of different systems of medicines, different socioeconomic status, it was imperative to have a standardized and robust pharmacovigilance and drug safety monitoring programme for the nation.

STRUCTURE AND FUNCTIONS OF PVPI:
The functional chart of PvPI is Pharma industry, healthcare professionals and patients are the major stakeholders of this programme. Any medicine or medicinal products approved for marketing in India by CDSCO, the concerned manufacturer is legally required to become the subject of post-marketing Periodic Safety Update Reporting (PSURs). PSURs are always more than an in-house assessment and directly submitted to CDSCO. The health care professionals collecting data of adverse events related to drugs marketed in India, can report to their respective ADRs Monitoring Centres (AMCs) which in turn is submitted to NCC through VigiFlow. The submitted data is collated and evaluated for quality by the various panels and groups of NCC-PvPI, IPC Ghaziabad. NCC is responsible for committing the reports to Uppsala Monitoring Centre (UMC) in Sweden and to communicate the scientific outcome to CDSCO for their regulatory intervention.

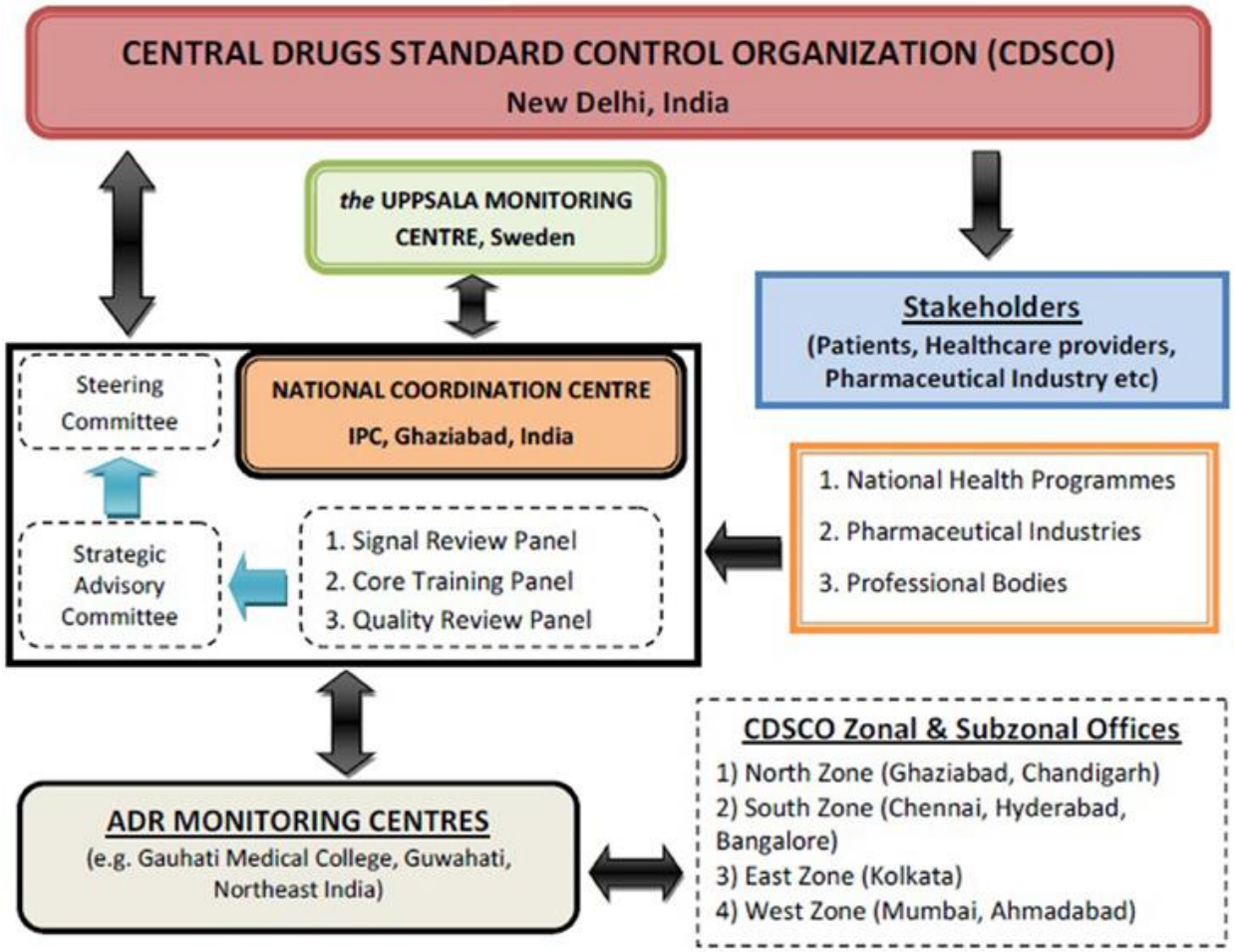

Fig no 2: Organogram of PvPI

SHORT TERM GOALS:

- To develop and implement Pharmacovigilance system in India
- To enroll, initially, all MCI approved medical colleges in the program covering north, south, east and west of India
- To encourage healthcare professionals in reporting of adverse reaction to drugs, vaccines, medical devices and biological products
- Collection of case reports and data

LONG TERM GOALS:

- To expand the pharmacovigilance programme to all hospitals (govt. & private) and centers of public health programs located across India
- To develop and implement electronic reporting system (e-reporting)
- To develop reporting culture amongst healthcare professionals
- To make ADR reporting mandatory for healthcare professionals

REPORTING ADVERSE DRUG REACTION:

Suspected ADR reporting forms for health care professionals and for consumers are unit available on the website of IPC to report ADR. To get rid of barrier in ADR reporting, the consumer reporting form are available in 10 vernacular languages (Hindi, Tamil, Telugu, Kannada, Bengali, Gujarati, Assamese, Marathi, Oriya, and Malayalam). ADRs will be conjointly reportable via PvPI helpline number (18001803024) on week days from 9:00 am to 5:30 pm. The mobile Android application for ADR reporting has conjointly been created available to the general public.

Version-1.2

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

For VOLUNTARY reporting of Adverse Drug Reactions by Healthcare Professionals

INDIAN PHARMACOPOEIA COMMISSION
(National Coordination Centre-Pharmacovigilance Programme of India)
Ministry of Health & Family Welfare, Government of India
Sector-23, Raj Nagar, Ghaziabad-201002

FOR AMC/NCC USE ONLY

AMC Report No. :

Report Type ☐ Initial ☐ Follow up

Worldwide Unique No. :

A. PATIENT INFORMATION

1. Patient Initials _____

2. Age at time of Event or Date of Birth _____

3. M ☐ F ☐ Other ☐

4. Weight_____Kgs

12. Relevant tests/ laboratory data with dates

B. SUSPECTED ADVERSE REACTION

5. Date of reaction started (dd/mm/yyyy)

6. Date of recovery (dd/mm/yyyy)

7. Describe reaction or problem

13. Relevant medical/ medication history (e.g. allergies, race, pregnancy, smoking, alcohol use, hepatic/renal dysfunction etc.)

14. Seriousness of the reaction: No ☐ if Yes ☐ (please tick anyone)

☐ Death (dd/mm/yyyy) ☐ Congenital-anomaly
☐ Life threatening ☐ Required intervention to Prevent permanent
☐ Hospitalization/Prolonged impairment/damage
☐ Disability ☐ Other (specify)

15. Outcomes

☐ Recovered ☐ Recovering ☐ Not recovered
☐ Fatal ☐ Recovered with sequelae ☐ Unknown

C. SUSPECTED MEDICATION(S)

S.No	8. Name (Brand/Generic)	Manufacturer (if known)	Batch No. / Lot No.	Exp. Date (if known)	Dose used	Route used	Frequency (OD, BD etc.)	Therapy dates		Indication	Causality Assessment
								Date started	Date stopped		
i											
ii											
iii											
iv											

S.No as per C	9. Action Taken (please tick)						10. Reaction reappeared after reintroduction (please tick)			
	Drug withdrawn	Dose increased	Dose reduced	Dose not changed	Not applicable	Unknown	Yes	No	Effect unknown	Dose (if reintroduced)
i										
ii										
iii										
iv										

11. Concomitant medical product including self-medication and herbal remedies with therapy dates (Exclude those used to treat reaction)

S.No	Name (Brand/Generic)	Dose used	Route used	Frequency (OD, BD, etc.)	Therapy dates		Indication
					Date started	Date stopped	
i							
ii							
iii							

Additional Information:

D. REPORTER DETAILS

16. Name and Professional Address:_____
_____
Pin:_____E-mail_____
Tel. No. (with STD code)_____
Occupation:_____ Signature:_____

17. Date of this report (dd/mm/yyyy):

Confidentiality: The patient's identity is held in strict confidence and protected to the fullest extent. Programme staff is not expected to and will not disclose the reporter's identity in response to a request from the public. Submission of a report does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the reaction.

Fig no 3: Suspected ADR reporting Form from Healthcare professionals

Version 1.0

MEDICINES SIDE EFFECT REPORTING FORM (FOR CONSUMERS)

Indian Pharmacopoeia Commission, National Coordination Centre- Pharmacovigilance Programme of India,
Ministry of Health & Family Welfare, Government of India.

1.Patient Details

Patient Initials: ☐☐	Gender (√): Male ☐ Female ☐ Other ☐	Age (Year or Month) :

2. Health Information

a. Reason(s) for taking medicine(s)(Disease/Symptoms):

b. Medicines Advised by (√): Doctor ☐ Pharmacist ☐ Friends/Relatives ☐ Self (Past disease experienced/No past disease experienced) ☐

3. Details of Person Reporting the Side Effect

Name (Optional):

Address:

Telephone No:	Email:

4. Details of Medicine Taking/Taken

Name of Medicines	Quantity of Medicines taken (e.g. 250 mg, Two times a day)	Expiry Date of Medicines	Date of Start of Medicines	Date of Stop of Medicines
			dd/mm/yy	dd/mm/yy
			dd/mm/yy	dd/mm/yy
			dd/mm/yy	dd/mm/yy

Dosage form (√) : Tablet ☐ Capsule ☐ Injection ☐ Oral Liquids ☐ If Others (Please Specify.....)

5. About the Side Effect

When did the side effect start? dd/mm/yy Side Effect is still Continuing (Yes/No): ☐

When did the side effect stop? dd/mm/yy

6.How bad was the Side Effect? (Please √ the boxes that Apply)

☐ Did not affect daily activities	☐ Affect daily activities
☐ Admitted to hospital	☐ Death
☐ Others	

7.Describe the Side Effect (What did you do to manage the side effect?)

This reporting is voluntary, has no legal implication and aims to improve patient safety. Your active participation is valuable. The information provided in this form will be forwarded to ADR Monitoring Centre for follow up. You are requested to cooperate with the programme officials when they contact you for more details. Please do report even if you do not have all the information.

Please turn the page to read the instructions

Fig no 4: ADR reporting form for consumers

Current status:

As on date, there are 60 AMCs spread across the four zonal offices of CDSCO are functioning under NCC. ADRs related to drugs, biologicals including blood and blood related products, recombinant DNA derived therapeutic products, vaccines and medical devices are being reported to these AMC's, in a specially designed ADR reporting form, which are transmitted to NCC after proper evaluation at each level. As on date, NCC committed total number of 20,750 ADRs to UMC. NCC is analyzing the data on monthly basis and the scientific outcome is communicated to CDSCO.

To develop the culture of voluntary reporting and to involve healthcare professionals and professional

associations in the drug monitoring and information dissemination processes, physicians, pharmacists, academicians and other healthcare professionals are being sensitized on the concept of pharmacovigilance and how to report ADRs through PvPI, across the country. As a part of promotional activities, CDSCO Zonal offices have written the letter to Medical and Pharmacy institutions to participate in PvPI. NCC has taken initiative step to publish PvPI Newsletter periodically and to circulate among the stakeholders nationally and internationally. The first Newsletter has been published on 2nd November 2011.

In order to provide training and technical support to the newly inducted AMCs, four Training and Technical Support Centres at regional level were identified by NCC. These include Post Graduate Institute of Medical Education and Research, Chandigarh (North), JSS Medical College, Mysore (South), Institute of Post Graduate Medical Education and Research, Kolkata (East), Seth GS Medical College and KEM Hospital, Mumbai (West). Keeping in view, the significance of this programme, an Appendix has been incorporated in 4th Edition of National Formulary of India 2011 and suspected ADR monitoring form also attached which may be filled in by the healthcare professionals and submitted to appropriate authority for further action. Thus it will help in rational prescribing and evidence-based regulatory decisions. The professional bodies/associations/organizations are encouraged to upload the suspected ADRs reporting form on their website. It will facilitate the easy availability of the form to the health care professional for ADR reporting

Future aspects:

Future Plan Steps have been taken to include Medical Council of India approved institutions and pharmacy institutions where having pharmacy practice and Pharm. D courses are being run under the fold of PvPI and further it would be expanded to all hospitals (govt. & private) and centres of public health programs located across India. Sensitization programme would be organized to train and encourage healthcare professionals in reporting of ADRs. Establishment of software for ADR database can be a worthy long-term goal in the Indian context

CONCLUSION:

The potential benefit of PvPI is aimed to reducing or eliminating a harm of medicine. The success of PvPI lies in its ability to prevent further ADRs on the basis of information received and the regulatory interventions. This can be achieved only when healthcare professionals are vitally alert to the onset or offset of any ADRs and ensure submission of quality data to the NCC, PvPI. Healthcare professionals and patients should come forward and actively participate to improving drug safety through ADRs monitoring in the country.

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