IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

An Overview of Pharmacovigilance Knowledge and Reporting System among Health Care Professionals

ARYA JAYAKUMAR[1*], DAWN V J[2], ARYA P[3], ASHA K S[4], PAVITHRA N[5], RAIHAN K T[6]

[12]Assistant Professor Department of Pharmacy Practice, [3456]B Pharm students, Nehru College of Pharmacy, Pampady, Thrissur.

Abstract:

Pharmacovigilance is one among the pillars of the Health Care system through assessment, monitoring and discovery of interaction among drugs and effect of drugs in human. A vital relationship exists between wide ranges of partners in the practice of drug safety monitoring such as industry, hospitals, government, patients etc. Sustained commitment and collaborations are important for future challenges in Pharmacovigilance are to be met in order to improve and flourish. Pharmacovigilance is well structured activity in the professional healthcare system, with dominant social and commercial implication that aimed at detecting and monitoring the risk or benefit ratio of medicines, improving quality and safety of the patient's life. Spontaneous reporting of ADRs and adverse events is the backbone of Pharmacovigilance system. Prevention of adverse drug reaction is the responsibility of doctors, pharmaceutical industry and patients. The true gains of Pharmacovigilance program could be achieved only when healthcare workers promote the habit of voluntary ADR reporting. It is a crucial step in preventing and reducing incidence of ADR. Some ADRs were negative impact of drug therapy. Self-medication, fake and adulterated medicines are the main burden of the ADR that expected to be even higher in developing countries. Aims of Pharmacovigilance involves to improve patient care and safety associated with the use of medicines,to improve public health and safety of medicines and to identify complications associated with the use of drugs. Patients have a crucial role in prevention of ADR by ensuring a high level of compliance with medical instructions which can minimize lethal effects of drugs. The fast and furious advancement of pharmaceutical and medical sciences has resulted in the accessibility of modern medicines that can prevent, control and manage disease states effectively.

Key Words:

Pharmacovigilance, ADR, Adverse event, Healthcare Professional, Knowledge, Reporting system.

INTRODUCTION

Pharmacovigilance is one of the pillars of the healthcare system through assessment, monitoring and discovery of interaction among drugs and effect of drugs in human beings. Fields of medicines like pharmaceutical and biotechnology are map out to cure, prevent, mitigate or treat diseases; although there are risks in particular Adverse Drug Reaction (ADR) can cause distress to patients. Thus, ADRs monitoring is having vital importance for safety of a medication.[1]

According to WHO, Pharmacovigilance as the "science and activities related to the detection, assessment, understanding and prevention of adverse effect or any other possible drug related problem". Healthcare professionals are defined as "Study, advice on or provide preventive, curative, rehabilitative and promotional health services based on an extensive body of theoretical and factual knowledge in diagnosis and treatment of disease and other health problems."[2] Adverse drug reactions are a response that is noxious and unintended that occurs at doses normally used in humans for the prophylaxis, diagnosis or therapy of disease or for modifying physiological function.[3]

Pharmacovigilance is the science gathering, monitoring, exploring, assessing and evaluating information from healthcare professionals and patients on adverse effects of the medications, blood and biological products, herbals, sera, vaccines, medical devices, traditional and complementary medicines with a view to spot new information about hazards associated with medications and preventing harm to patients. Challenges of maximizing drug safety and maintaining public confidence has become increasing. Complex pharmaceutical companies must not only monitor, but also proactively estimate and manage drug risk throughout a products lifecycle, from its developing stage to post market drug safety monitoring, it is an essential part for the effective use of medicines and for high quality medical care. It has the possibility to encourage confidence and hope among patients and health professionals in medicines and contributes to raising quality of medical practice.. Health care

practitioners are in position to make good use of their patient's positive and negative experiences of treatment to contribute to medical science and to an improved understanding of disease and medicines.

A vital and complex relationship exist between wide ranges of partners in the practice of drug safety monitoring such as industry, hospitals, government, health care centres, patients etc. sustained commitment and collaboration are important if future challenges in pharmacovigilance are to be met in order to improve and flourish.

In the past, there was no major compulsion to have a strong pharmacovigilance system to detect and monitor ADRs of marketed products when hardly any new drug was launched for the first time in India. Experiences from the markets where the drugs where in use for many years before its introduction in India was used by the companies and regulatory agency to assess the safety parameters and take corrective actions like banning of drug or withdrawal.

The discipline of pharmacovigilance has emerged considerably since 1972, WHO technical report and it retains a dynamic clinical and scientific discipline. Critical to meet the challenges of the increasing range and potency of pharmaceutical and biological medicines that includes vaccines, which carry with them and inevitable and somewhat unpredictable potential to harm. The menace of harm, however is less when medicines are used by an informed health professionals and by patients, who themselves understand and share responsibility for their drugs. When toxicity and adverse events appears, especially when previously unknown in association with the drugs, it is important that they are analysed and communicated effectively to a public that has the knowledge to interpreting the information. This is the role of pharmacovigilance of which much has already been procured. But more efforts required for the integration of the discipline in to the clinical practice and public policy.

Spontaneous reporting of ADRs and adverse events is the backbone of Pharmacovigilance system. Spontaneous report is an unprompted communication by healthcare professionals to a regulatory authority, company or other organization that describes one or more ADRs in a patient who was given medicines and that doesn't derive from a study or any organized data collection scheme. Spontaneous reports place a vital role in the identification of safety signals of a marketed drug. Spontaneous reporting of ADRs is a vital tool for gathering the safety information for early detection. The advantage of spontaneous reporting that it is available immediately after a new product is marketed is continued indefinitely and cures all patients that receive the medicines. Spontaneous reporting is the most suitable method for detecting rare and new ADRs and frequently evolves safety signals which need to be examined further. It is a passive approach to Pharmacovigilance relying entirely on the motivation of individuals to report suspected ADR to a local or national Pharmacovigilance centre. Spontaneous reports can be electronic or paper based from multiple CCSRS is used to identify potential 'signals'- suggestions of casual associates between a medical product and a previously unknown reaction. The predominant features of reporting is that they cover all medicine use within a while population for a unlimited period of time, enclosing the entire lifecycle of the each medicinal products. The intrinsic merits of spontaneous reporting more over active reporting methods, the wide coverage mean rare, serious ADRs are not detecting during earlier trials or through other methodologies may be revealed indeed. Spontaneous reporting is crucial step for preventing or reducing ADRs and all the health care professionals are responsible for that reducing ADRs and cost effective surveillance system are cornerstones of safety monitoring of the medicine in clinical practice. Few studies have focused on the effect of the intervention to improve the ADR reporting all over the world.[4]

The true gains of Pharmacovigilance program could be achieved only when healthcare workers such as doctors, nurses, pharmacists promote the habit of voluntary ADR reporting. It is a crucial step in preventing and reducing incidence of ADR. Some ADRs where negative impact of drug therapy. Self-medication, fake and adulterated medicines are the main burden of the ADR that expected to be even higher in developing countries.

Aim and Objectives

- To improve patient care and safety associated with the use of medicines.
- To improve public health and safety of medicines.
- To identify complications associated with the use of drugs and conveying it a suitable manner.
- To evaluate advantage efficacy and risk of medicines as well as promoting safe, rational and more effective use of medicines.
- To encourage education understanding and clinical training in Pharmacovigilance along with its effective communication to the healthcare workers and public.

Role of Pharmacovigilance

Pharmacovigilance is specifically concerned with ADRs. Incessant monitoring of effects of drug, side effects, contraindication and outright adverse effects which could result in a drastic degree of morbidity and in some cases even mortality are essential to maximize benefits and reduce risks. The drug regulatory agencies hence the responsibility of having a well-established Pharmacovigilance system for monitoring ADRs during the life time of marketed product from drug development phase and to finished product.

History of Pharmacovigilance

Pharmacovigilance started about 170 years ago although it was not yet named as such at that time. It is well structured activity in the professional health system, with dominant social and commercial implication that aimed at detecting and monitoring the risk or benefit ratio of medicines, improving quality and safety of the patients life. In this commentary we report the milestone of Pharmacovigilance up to the present scenario, in order to recollect the entire steps that have characterized historical evolution, from the initial reports, which are essentially letters or warnings sent by health care professionals to publishers of famous scientific journals, up to today's modern and ultra-unique structured electronic registries. Pharmacovigilance help us to achieve such important results for man's health and pharmacology itself, and to interpret the challenges that await pharmacovigilance in upcoming years are clearly depicted from the historical phase. On 1848 January 29, a young girl (Hannah Greener) from north England died after administering chloroform anaesthetic before removal of an infected toenails. Sir James Simpson had discovered that chloroform was a safer and powerful anaesthetic, and he had introduced it in clinical practice. The causes of Hannah's death were investigated to understand what happened to Hannah, but it was impossible to identify what killed her. Probably she died of a deadly cardiopathy or respiratory organ aspiration. As a result of other deaths raised by the clinicians and the public about the safety of anaesthesia, The Lancet Journal established

a commission to confront this problem. The commission incited English doctors, including the doctor in colonies, to report deaths caused by the anaesthesia.

The US Federal Food and Drug Act were formed on June 30, 1906, to establish that drugs must be pure and free of any contamination. Moreover, in 1911, this organization prohibited false therapeutic indications of drugs. In the year 1937, 107 deaths were reported in the USA, because of the use of sulphanilamide elixir, containing diethyl glycol used as solvent. This solvent was considered the cause of deaths, but the manufactory companies were not aware about its toxicity at that time. As a result, the Federal Food, Drug and Cosmetic Act were established in 1938; its aim was to upgrade the public health system. Indeed, the new system anticipated that the safety of drugs should be demonstrated before their market approval, and introduced the possibility of conducting factory inspections. In 1938, Douthwaite supposed that acetylsalicylic acid (ASA) could cause Melena. In 1955, ASA cause GI diseases so that it is currently contraindicated in patients with gastrointestinal ulcers.

In 1961, a major change of European Pharmacovigilance happened after the tragedy of Thalidomide. A retrospective study conducted on 1973 showed that correlation between the congenital malformations of babies and the use of thalidomide during pregnancy. This tragedy convert the system of Pharmacovigilance, as the spontaneous reporting of ADR became systematic, organized, and regulated. "Yellow card" (YC) was structured in the UK ON 1964, it is a specific form to systemize a spontaneous report of drug toxicity. In Europe the disaster of thalidomide promoted the development of a European legislation with the EC Directive 65/65 on 1965.

In 1968, the WHO Programme for International Drug Monitoring was introduced and ten members take part in this program (Australia, UK, USA, Germany, Canada, Ireland, Sweden, Denmark, New Zealand, and Netherlands). Italy participated in this program in 1975. In 1992, the European Society of Pharmacovigilance (ESoP) was funded, changed to the International Society of Pharmacovigilance (IsoP). The focus of this society were to upgrade Pharmacovigilance, and improve all characteristics of the safe and proper use of medicines. The European Medicines Agency (EMA) was established on 1995. In 2001, EudraVigilance was funded. It is the official European database for managing and analysing information on suspected adverse reactions to medicines which have been authorized for the market or being studied in European clinical trials. A foremost change in European Pharmacovigilance was witnessed with the new legislation (Directive 2010/84/EU), in 2012.

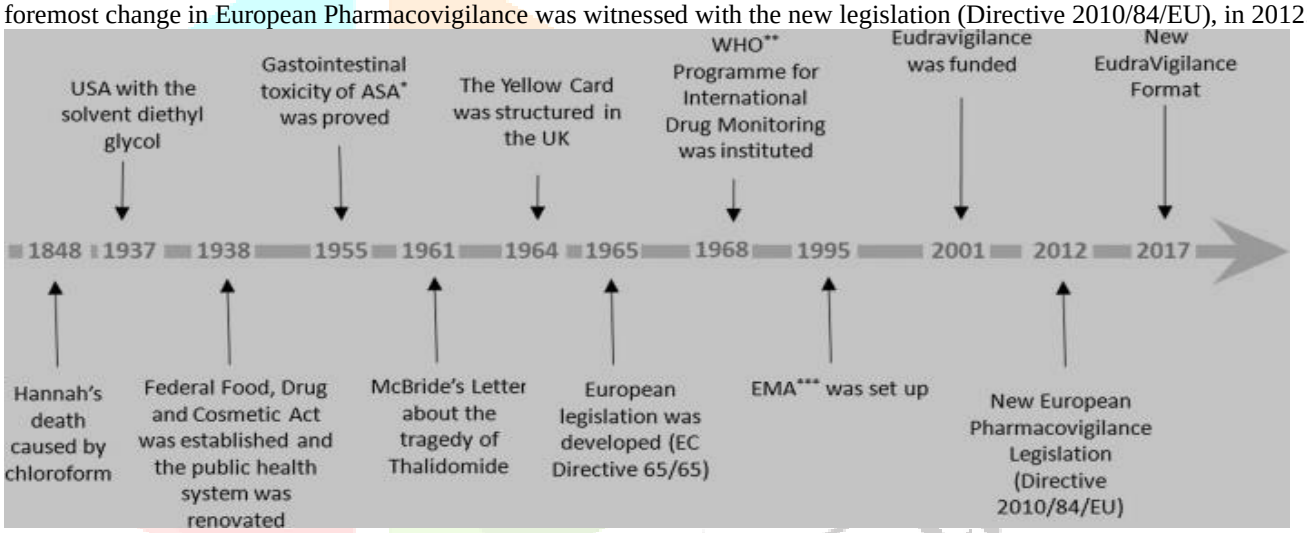


Fig.1 Timeline of the historical evolution of Pharmacovigilance. *ASA: acetylsalicylic acid; **WHO: World Health Organisation; ***EMA: European Medicines Agency

Moreover, the new legislation set-up considers facilitating the performance of PV, called the Good Pharmacovigilance Practices (GVP). The GVP guideline is divided into two classes: modules covering major Pharmacovigilance processes and product- or population-specific considerations. This last class is available for vaccines and biological medicinal products. In this guideline there are also special chapters dedicated to special areas, namely pregnancy and breast-feeding (P III) and geriatric population (P V).

In November 2017, the new EudraVigilance format was launched; in particular, the marketing authorizations will have extended access to the EudraVigilance database to support the attainment of their Pharmacovigilance obligations. This last category is out there for vaccines and biological medicative merchandise. During this guideline there are special chapters dedicated to special areas, specifically maternity and breast feeding (P III) and geriatric population (P V).[5]

Pharmacovigilance in India was originated in 1986 with an official adverse drug reaction (ADR) monitoring system, under direction of the drug controller of India. India joined the World Health Organization (WHO) Programme based in Uppsala, Sweden. This attempt was unsuccessful and hence, from 1 January 2005, the WHO sponsored and World Bank-funded National Pharmacovigilance Program for India was made functioning. It was to be superintended by the National Pharmacovigilance Advisory Committee based in the Central Drugs Standard Control Organization (CDSCO), New Delhi. Two zonal centres the South-West zonal centre (situated in the Department of Clinical Pharmacology, Seth GS Medical College and KEM Hospital, Mumbai) and the North-East zonal centre (situated in the Department of Pharmacology, AIIMS, New Delhi), were to collect and combine information from all over the country and send it to the Committee as well as to the Uppsala monitoring centre in Sweden. Three regional centres would report to the Mumbai centre and two to the New Delhi one. Every regional centre in turn would have some peripheral centres reporting to it. Presently there are 26 peripheral centres. The program has three extensive objectives: the short-term objective is to encourage a reporting culture, the intermediate objective is to involve a large number of healthcare professionals in the system in information dissemination and the long-term objective is for the program to be a benchmark for global drug monitoring. [6] In 2010 National Programme of Pharmacovigilance was renamed as Pharmacovigilance Programme of India (PvPI). [7]

Adverse Drug Reactions

As per World health Organization adverse drug reaction is defined as "any response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function"[8]. Adverse reactions may arise from use of the product within or outside the marketing authorisation or from occupational exposure.[9] Adverse drug reactions are considered as one among the leading causes of morbidity and mortality. Pharmacovigilance is the field concerned with the study of ADR.[10]

Importance of Adverse drug reaction:

Adverse drug reactions are a major clinical problem. The various effects of adverse drug reaction are:

- Adverse effect based on patients quality of life
- Admission to hospitals
- Cost of patient care gets increased
- Length of hospital stay gets increased
- Patient may lose confidence in their treating doctor[11]

Classification of Adverse Drug Reaction

S.NO.	Classification of ADR	Features	Examples
1	Type A (Augmented)	• Relatively common • Pharmacologically predictable • Dose related • Improves if medicine is withdrawn	• Hypoglycaemia with sulfonylureas • Insulin induced hypoglycaemia • Bradycardia
2	Type B (Bizarre)	• Involves interaction with a microorganism • Pharmacologically predictable • Improves if medicine is withdrawn	• Dental caries with sugar coated tablets • Resistance due to overuse of any one antibiotic • Penicillin induced hypersensitivity reaction
3	Type C (Chemical)	• Related to drug concentration • An irritant reaction	• Extravasation reactions • phlebitis
4	Type D (Delivery)	• Caused by method of administration or nature of formulation • Improves if medicine is withdrawn or method of delivery is changed	• Inflammation or infection around implant particles • Infection at site of injection
5	Type E (Exit)	• Pharmacologically predictable • Begins when the medicine is stopped or dose is reduced • Improves if medicine is reintroduced	• Withdrawal reactions due to opioids , clonidine
6	Type F (Familial)	• Occurs only in the genetically predisposed	• Haemolytic anaemia with primaquine in G6PD deficient individuals
7	Type G (Genotoxicity)	• Causes irreversible genetic damage	• Teratogenic agents like thalidomide causing genetic damage in the foetus
8	Type H (Hypersensitivity)	• Requires activation of immune system • Improves if medicine is withdrawn	• Anaphylaxis with penicillin • Allergic skin reactions with antimicrobial agents
9	Type U (Unclassified)	• Mechanism is unknown	• simvastatin use causes taste disturbances • Nausea and vomiting with gaseous anaesthetic[15]

Table.1 Classification of ADR

Preventing Adverse Drug Reaction

Prevention of adverse drug reaction is the responsibility of doctors, pharmaceutical industry and patients. Patients have a crucial role in prevention of ADR by ensuring a high level of compliance with medical instructions which can minimize

therapeutic effects. Inadequate compliance can lead to toxicity or treatment failure and thereby increase treatment costs and possible fatal outcome for the patient.[12]

Detection of Adverse Drug Reaction
Various detection methods of ADR are

1. Pre-marketing studies
2. Post-marketing surveillance
3. Assessing Causality
4. Communicating ADRs
5. Postal survey method

1. Pre-marketing studies:
   The safety test of new formulated medicines is done on animal models.3 distinct phases of clinical trials are performed before submitting final report to a marketing authorization application (MAAP)
2. Post marketing surveillance:
   Subsequent to the approval of the product, new drugs should be closely monitored for their clinical safety once they are marketed. PSURs shall be submitted every 6 months for the 1st 2 years after the approval of drug is granted to the applicant. For subsequent 2 years the PSURs shall be submitted annually. All serious unexpected adverse reaction cases must be reported to the licensing authority within 15 days of initial receipt of the information by the applicant.
3. Assessing Causality:
   Causality assessment is a process of establishment of a relationship between a drug and a suspected reaction. In case an ADR is suspected then the assessment starts with the collection of the relevant data related to patients demographic like medications including OTCs time of onset and duration of reaction; treatment of reaction and its outcome.
4. Communicating ADRs:
   Knowledge about national and safe use of medicines are provided at time of basic training of health professionals ,by conducting constant education programmes for health professionals, by inserting package and by counselling patient as well.
5. Postal survey method:
   This method consists of specific drug related questionnaire used for monitoring ADR of new drugs i.e. within 1 to 2 years after the drug has been launched. The questionnaire should inquire the details about drug, usage, dose, brand used, and number of patients treated in a given period. Questionnaire including a prepaid envelope should be mailed to medical practitioners all over the city/state who are likely to use the drug. [13]

Management of Adverse Drug Reaction:
Stepwise approach to manage ADR
Step 1:

- Assess the severity of ADR (eg: anaphylaxis, hypersensitivity)

Step 2:

- Adjust the therapy
  1. Reduce the dose
  2. Withhold the dose
  3. Stop Rx

Step 3:

- Initial supportive treatment for ADR/ antidotes
- Refer for specialist/ acute care; if required

Step 4:

- Assess clinical parameters

Step 5:

- If adjusting Rx resolves ADR; continue modified regimen
- If stopping Rx resolves ADR; consider alternative Rx:-
  1. If “therapeutic group” effect: consider alternative pharmacological class
  2. If “drug specific” effect: consider different agent in the same pharmacological class and monitor for cross section
  3. Consider alternative formulation

Step 6:

- If ADR persist: explore other causes

Step 7:

- If Rx essential; and no alternative regimens- consider desensitization regimen[14]

Reporting of Adverse Drug Reaction:
Reporting of an adverse drug reaction (ADR) is one of the most important parameter of medical treatment. It helps in evaluating safety of drug therapies, especially of those drugs that are approved recently. It also offers updated drug safety information to health care professionals and other stakeholders.

Who can report:
All healthcare professionals including clinicians, dentist, pharmacist, nurses, physician, physiotherapist and non-healthcare professionals including consumers, patients can report.

When to report:
ADR should be reported immediately and report can be incorrect and unreliable if the ADR reporting is delayed.

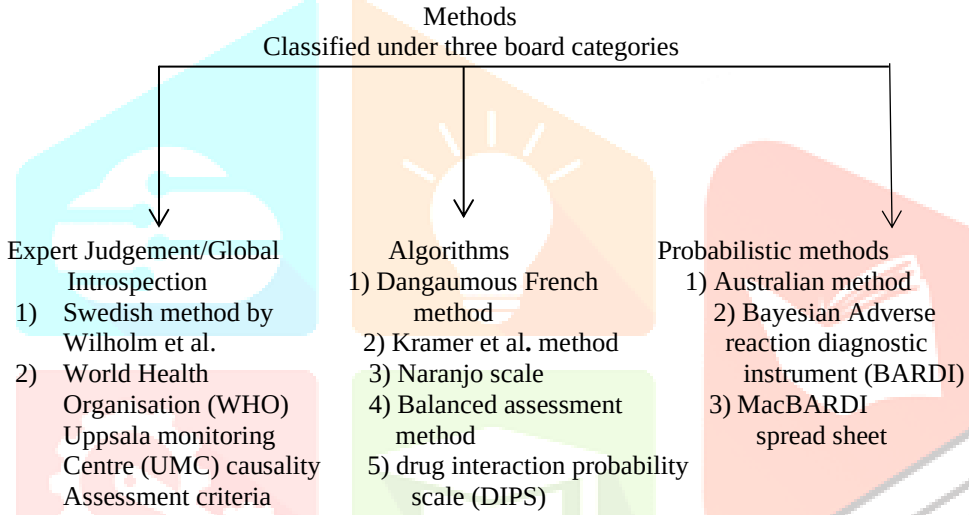
How to report:

- Standardised ADR reporting form should be used for reporting
- Separate forms with complete information should be used for every individual
- Completely filled ADR form should be then returned to nearest adverse drug reaction monitoring centre (AMC) or to National Coordinating Centre
- Any follow-up information should be forwarded by another ADR form, in case of an ADR case that has been reported already.[15]

Causality Assessment

Causality assessment can be defined as the assessment of relationship between the treatment with any drug treatment and incidence of an adverse reaction. Causality assessment is an important part of ADR reporting system and important task, conducted by National Pharmacovigilance Programme in every country. [20].
Methods of causality assessment:
Many researchers developed various methods of causality assessment by using different criteria like:

- Chronological relationship between the administration of the drug and therefore the incidence of the ADR,
- Screening for drug and non-drug connected causes,
- Confirmation of the reaction by in vivo or in vitro test,
- Previous information on similar events.



A. Expert judgement / Global Introspection
These are individual evaluation on basis of previous knowledge and experience in the field. Judgements are made without using any standardized tool for getting conclusions regarding causality. Adverse drug reaction is assessed either by individual expert evaluator or by a group of evaluators.

B. Algorithms:
Algorithms are a set of queries with associated scores for calculating the probability of a cause-effect relationship. It consist of a problem specific flow chart with step-by-step instruction on how to arrive to an answer.

1. Dangaumou's French method:
scores are clustered into likely, possible and dubious in this method. This method uses seven criteria in two different tables: 3 chronological and 4 semiological
   i. the chronological criteria are :
      - Drug challenge
      - Dechallenge
      - Rechallenge with an overall score of four possible categories
   ii. The semiological criteria are :
      - Semiology
      - Favouring factor
      - Alternative non-drug-related explanation
      - Specific laboratory test with three possible outcomes
2. Kramer et al. method:
In this method algorithm is applied to a single clinical exhibition that can occur after administration of a single suspect drug. When multiple drugs are involved, every drug can be evaluated separately. Transparency of algorithm is one of its advantages.

3. Naranjo et al. method (Naranjo scale):
This method is widely accepted and it facilitates in determining the likelihood of whether an adverse drug reaction (ADR) is actually due to the therapeutic drug rather than other factors result. It consists of 10 questions that are

answered as "yes", "no" and "unknown". These answers are assigned by a score term as: Definite, Probable, Possible and Doubtful.

i. Definite- when a total score of ≥ 9
ii. Probable- when a total score of 5-8
iii. Possible- when a total score of 1-4
iv. Doubtful- when a total score

4. Balanced assessment method:
In this method, the case reports are evaluated on a series of visual analogue scales (VAS) based on the possibility of fulfilling each condition.

C. Probabilistic method:
This methodology is employed in case of specific findings whereas remodelling the estimate of prior probability into posterior probability of drug causation. With the information, prior probability can be calculated and posterior probability combines with the previous information along with the evidence of the particular case to find out an approximate of causation.

i. Australian method: One of the first probabilistic methods used. In this method the conclusions can be drawn based on internal evidence. While proceeding in the evaluation process, previous knowledge on the suspect-drug profile is purposely excluded.
ii. Bayesian Adverse Reaction Diagnostic Instrument (BARDI):It is established to overcome the numerous limitations allied with expert judgements and algorithms and used for calculating odds of a specific drug by comparing adverse event with an alternative cause.
The five likelihood ratios (LR):
1. Patient history (Hi)
2. Timing of the adverse event with respect to drug administration (Ti)
3. Characteristics of the adverse event (Ch)
4. Drug dechallenge (De)
5. Drug rechallenge (Re)[16]

Pharmacovigilance- Regulatory Agencies and Organisations

As the pharmaceutical industries throughout the world are moving ahead towards becoming more and more competitive, regulatory agencies are being established in various countries across globe. Regulatory bodies and organization play a vital role to meet the requirement of legal procedure related to drug development process in a country. In present scenario, pharmaceuticals are considered as the most regulated industries worldwide and where Drug regulatory and Pharmacovigilance are essential part of the larger health care industry. Drug regulatory authorities play a key role in National or regional oversight of Pharmacovigilance and different countries have their own regulatory authority ,which is responsible to enforce the rules and regulations and issue the guidelines to regulate drug development process ,licensing ,registration ,manufacturing ,marketing and labeling of pharmaceutical product.

USFDA(USA) MHRA(UK) ,CDSCO(INDIA),SFDA(CHINA),KFDA(KOREA),SWISMEDIC(SWITZERLAND) are the few regulatory agencies and organization established in respective countries.[17]

United States : In the U.S ,with about a third of all global 2011 pharmaceutical expenditure the drug industry is regulated by the FDA ,they are exercised through enforcement of regulatory derived from legislation published in the US code of federal regulation .The principal drug regulation is found on 21CFR proof and 21CFR part 314. Those regulatory efforts address pre marketing concerns ,In US RADAR and Public citizen do play a role in pharmacovigilance in the US.[18] The FDA are also the statuary authority involved in response to drug related public health crises and the response to a changing environment . The social, health care environment changed and continues to involve health care provider expert timely access to effective drugs, the program established in 1992 has increased pace of drug review and approval practice of medicine and the drug have changed available information to the public form advertising, internet from commercial government or nonprofit role in healthcare.

In view of these changes the regulatory agency should be reconsidered and made stronger to ensure that it is task to equal; The committee, considerable new resource to perform optimally in a fast-changing challenging environment, such as DTC advertising and stay training and expertise in drug regulation.[19]

European Union: Pharmacovigilance in the EU is coordinated by the European medicines agency and are conducted by the national competent authority, the authority responsible for to maintain and develop the Pharmacovigilance database consisting of all suspected serious adverse reaction to maintain to medicine observed in the European community. The European medicines agency require the individual marketing holder to submit all received adverse reaction in electronic form ; except in exceptional circumstance .[20]

Japan: In Japan, Pharmacovigilance matters are regulated by the pharmaceutical and medical device agency and the ministry of health Labor and welfare [21]

Canada: In Canada ; Pharmacovigilance regulated by the market health product directorate of the health product and food .Canada was second following the US in the holding the highest total prescription drug expenditure per capita in 2011 at around US dollar per person . In august 2017, there was government controversy in which a bill, known as Vanessa law, to protect patient from potentially dangerous prescription drugs was not being fully realized by hospital. [22]

Who International Drug Monitoring Program:

WHO program for international drug monitoring was started in 1968. Firstly a plot project in 10 counties with recognized national reporting system for ADR, the network has since expanded significantly as more countries worldwide developed national Pharmacovigilance centers for the recording of ADR. Currently 86 countries participated in Programme, which is coordinated by WHO together with its collaborating center in Uppsala, Sweden [23].The collaborating center is responsible for maintaining the global ADR database, vigibase. The program consists of a three parts networks:

1. National Pharmacovigilance centers from WHO members countries are responsible for case reports sent to the WHO ICSR data base
2. UMC oversees the WHO program operation, including collecting, assessing and communicating information from member countries about the benefits, harm, effectives, and risk of drugs.
3. Collaborating with members countries in the development and practice of pharmacovigilance.
4. Alerting NRA of member's countries about potential drug safety problems via the WHO signal process.
5. WHO headquarters in Geneva, Switzerland is responsible for policy issues.

The national Pharmacovigilance center will be responsible for the development of pharmacovigilance in the public health care system, will promote Pharmacovigilance in the PHPs and sensitize professional and public health staff to the reporting of adverse reaction and irrational use of medicines.

WHO promotes PV at country level, initially the WHO PIDM members consist of 10 countries. As of January 2016,123 countries have joined the WHO PIDM and in addition 28 associate members are awaiting full members.

WHO PIDM members state submit reports of adverse reaction associated with medical product ,known as individual case safety reports to the WHO global database , vigibase. Where vigibase is managed by the WHO collaborating center for international drug monitoring known as the Uppsala monitoring center. In October 2014 there were over 10 million reports of adverse reaction in vigibase. The aim of pharmacovigilance are of to enhance patient care and patient safety in relation to the use of medicines and to support public health Programme by providing reliable ,balanced information to assess the risk - benefit profile of medicines.

Uppsala Monitoring Center Role as a WHO Collaborating Center: UMC is one of the four officially designed collaborating center with in the WHO program for international drug monitoring .UMC is responsible for managing the technical and scientific aspect of the WHOs worldwide pharmacovigilance networks .These activities are carried out following WHO policy and in close liaison with headquarters in Geneva . They included:

- Collecting, assessing and communicating information from member countries about the benefits, harm , effectiveness and risk of medicines
- Analyzing vigibase data and identifying signals of potential safety problems
- Collaborating with member countries in the development and practice of pharmacovigilance through consultation and training
- Pursuing research in all aspect of the science and practice of pharmacovigilance
- Being a partner in the extended global patient safety network.[24]

Pharmacovigilance Program of India

As part of PVPI ,ALL INDIA INSTITUTE OF MRDICAL SCIENCE (AIIMS) ,New Delhi selected as National coordinating center(NCC) to safe guard public health by validating the safety of products .About 22ADR monitoring centers were established in the year 2010 .The NCC was transferred from AIIMS New Delhi to IPC and Ghaziabad on 15 th April 2011 for smooth and efficient functioning of program .selected eligible medical colleges ,hospitals ,and centers were approved as ADR monitoring (AMCs) These AMCs collect the individual case safety (ICSRs), analysis and report it to regulatory the authority .Till January 2017 ,250 AMCs have been established.

About 20 anti-retroviral therapy and 17 revised national tuberculosis program (RNTCP) centers were also established for spontaneous ADR reporting .The technical associate from medical science ,Banaras Hindu university is an authorized person for collecting ICSRs along with its follow up and online database entry in vigi-flow software .It was considered that the remedies from natural sources are safe and devoid of ADR .But Charka Samhita ,Which is the heart of ayurvedha illustrate that ADR can occur with herbal drug also if they are compound and dispensed inappropriately .[25]

Where CDSCO, the central drug standard regulatory body for cosmetics, pharmaceutics and medicinal devices. It serves a similar function to the FDA, NMPA. The Indian government has announced its plan to bring all medical devices, including implants and contraceptives under a review of the central drug and standard control organization .Within CDSCO Where DGCI controls the pharmaceutical and medical devices within Ministry of health and family welfare. [26]

Current Trends in Pharmacovigilance

The fast and furious advancement of pharmaceutical and medical sciences has resulted in the accessibility of modern medicines that can prevent, control and/or manage disease states effectively. Despite a surfeit of benefits, adverse reactions to medicines are not unusual and are linked with most newly developed medicines. The International Drug Computer Program was formed by the World Health Assembly. Inputs from the variety of sources such as, academia, government, pharmaceutical and medical associations, health professionals and the media will help towards achieving improved management of risks associated problems associated with the use of medicines. Pharmacovigilance is constituted, and justified therefore, in many areas of healthcare management of general population. The key areas where pharmacovigilance is incorporated are, National Drug Policy: For all nations, the first step to ensuring safety and rational use of medicine is the establishment of drug regulatory bodies with eminent pharmacovigilance programs to monitoring and assessing the adverse drug reactions and communicate finding to relevant stakeholders. Pharmacovigilance programs in clinical practice helps health care professionals to continuously updating and remain current knowledge related to adverse outcomes of medicines. Several developing and underdeveloped countries lack a well-organized and efficient healthcare infrastructure and countries have high prevalence of tropical infectious diseases; most of them existing concurrently in a population. Simultaneously the administration of several medicines to such population is often carried out without regards to or knowledge of the adverse drug reactions or drug interactions. Pharmacovigilance programs in such situations there is need of adequate training to the healthcare professionals and helps to improve general awareness regarding the safe use of drugs. Several international and national bodies provide information and guidelines for proper implementation of pharmacovigilance programs all over the world. These agencies are excellent resources for information on the management of risks associated with the usage of drugs. World Health Organization (WHO) provides a comprehensive database of information on the adequate implementation of pharmacovigilance as an important tool to ensure the safety of medicine in public health. [27]

Current Scenario of Pharmacovigilance in India:

India is a vast developing country and there is abundance of drug brands—proudly more than 6,000 licensed drug manufacturers and over 60,000 branded formulations of drugs. India is the fourth largest producer of pharmaceuticals in the whole world. Bundles of new drugs are being launched in the country, so there is an drastic urge for improvement in pharmacovigilance system to ensure safety to the Indian population from serious harm that may be caused by certain new medications. Indian based pharma companies have increased their potential to develop and launch new pharmaceuticals through their own research efforts and this has increased the importance of developing adequate internal pharmacovigilance standards to detect adverse drug events. However, what needs to be vital along with the funding is the focused mission and effective strategy for developing the pharmacovigilance systems, especially in the Drug Controller General of India (DCGI) Office, which is lacking. Traditionally, pharmacovigilance was never done in India in pharmaceutical companies, be it Indian or Multi-National Companies (MNCs), so there is an immense shortage of knowledge people who could able to advice the DCGI on this matter, where pharmacovigilance is a very complex subject, intertwined with many regulations and complex systems. Therefore the need to engage a completely independent adviser who has extensive and practical knowledge on pharmacovigilance, who can act as Pharmacovigilance Advisor to the Government of India to effectively implement the systems and policies on pharmacovigilance.Understanding by healthcare professionals and knowledge and motivation for pharmacovigilance is almost negligible. In India, several consumer groups encourage patients to report any ADRs encountered by them, although there is no information for patients on how to report ADRs directly to the regulatory authority. Direct reports from the patients, the ones who actually experience ADRs, are not accepted by the monitoring centers and by regulatory authorities. With many clinical trials and other clinical researches that conducted in India to understand the importance of Pharmacovigilance. At present, the DCGI should quickly to access pharmacovigilance so as to merge Good Pharmacovigilance.

Currently India is considered to be a pivot for clinical research. The DCGI has shown its commitment to ensure safe usage of drugs by establishing the National Pharmacovigilance Program.Consumers,healthcare professionals, Non-governmental organisations as well as hospitals should appreciate that recently a system in place to collect,analyze and monitor the adverse event data. They should intentionally report adverse events actively and participate in the National Pharmacovigilance Program to ensure that people in India receive safe quality medicines. With the immense hard work and proper coordination of all stakeholders, we can definitely build a world class Pharmacovigilance system in India. It may results to tremendous advancement in this field.

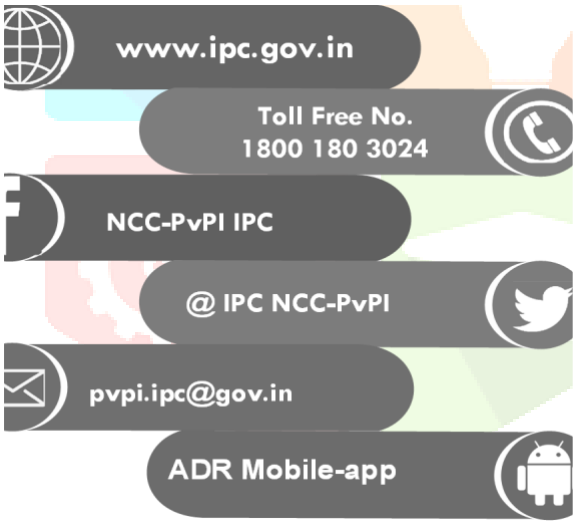


Fig.2 Connect and contact us

The Future of Pharmacovigilance:

The main goal of Pharmacovigilance is to influence healthcare professionals and patients to use drugs safely. Companies spend dollars and dollars on Pharmcovigilance every year aiming to achieve the goals. Adverse drug reactions (ADRs) remain a major cause of death. In fact, ADRs account for hospital admissions. Recently this is major challenges for pharmaceutical companies. Hoggishly regulated organizations of PV to face pressure to analyze datas, monitor risks more carefully and accurately report every known patients event around the world. Handling individual case safety reports particularly consumes immense resources. Ultimately, the pharmaceutical companies will have no choice but to migrate to an automated case-processing model in the upcoming years. But to be truly effective influencers, pharmaceutical companies must build trust and confidence recent public surveys indicate that the pharmaceutical companies are among the most distrusted. Advanced solutions can already automatically extract, process, and code adverse effect data. Emerging tools will leads to greater openness across the pharmaceutical companies and promote impartial comparisons of alternative pharmaceuticals products. This will drive more collaboration, trust and ultimately less ADR. Signal management tools will scrape the web for meaningful data of particular medicines. This system will automatically identify the analogues based on logical constructs like therapeutic area, drug class and less intuitive factors. [28]

Conclusion

Health Care Professionals have good perception about ADR and its reporting system. However, the implementation of the knowledge into practice is lacking mainly due to lack of awareness of National Pharmacovigilance program running currently

in the country. Even the experienced Health professional staffs have a lack of experience to bound the theoretical knowledge into practical one and they are unaware of what further happens on reporting of ADR Forms , still they have reported ADR cases in their practice time as health professional . And these situations could be dealt by providing to the Health care professionals with an educational and awareness programs.

Acknowledgment
We like to express our deepest thanks to our parents, teachers and almighty.

References

1. Dhara R Sanghavi, Priti P Dhande, Vijaya A Pandit. Perception of Pharmacovigilance among doctors in a tertiary care hospital: influence of an interventional lecture. Int J Risk Saf Med. 2013; 25(4): 197-204.
2. The importance of pharmacovigilance – safety monitoring of medicinal products. Geneva: World Health Organization; 2002 (http://apps.who.int/medicinedocs/en/d/Js4893e, accessed 22 May 2018)
3. International drug monitoring: the role of national centres. Geneva: World Health Organization; 1972 (http://apps.who.int/iris/handle/10665/40968, accessed 22 May 2018).
4. Sanvidhan G Suke, Prabhat Kosta and Harsh Negi. Role of Pharmacovigilance in India : An overview, online J Health Inform-2015,7(2):e223.
5. Giulia Fornasier, Sara Francescon, Roberto Leone & Paolo Baldo. A historical overview over pharmacovigilance. International Journal of clinical pharmacy-40,744-747(2018).
6. V Kalaiselvan, Sushma Srivastava, Abhishank Singh, S K Gupta.Pharmacovigilance in India: Present Scenario and Future Challenges.Drug saf.2019Mar;42(3):339-346.
7. Kumar A. Past, Present and Future of Pharmacovigilance in India.Review Article 2010Sep.
8. WHO (1972) International drug monitoring: the role of national centres. Technical report series WHO 1972, no 498.
9. https://www.chiesi.fr/en/pharmacovigilance
10. http://www.mhra.gov.uk/yellowcard
11. SK Gupta, Post marketing Surveillance. Textbook of Pharmacovigilance, First edition, Jaypee Brothers Medical Publishers (P) Ltd., 2011;40.
12. https://www.slideshare.net/DrVijayBhushanam/vj-ad-rs
13. M C Gwee. Ann Acad Med Singap. Prevention of adverse drug reactions: role of the patient (consumer).
14. The World Health Organization. Safety of Medicines; A guide for detecting and reporting adverse drug reactions. Geneva: 2002 WHO/EDM/2002.2.
15. Rehan HS, Vasudev K, Tripathi CD. Adverse drug reaction monitoring: the knowledge, attitude and the practices of the medical students and prescribers. Natl Med J India.2002 Jan-Feb; 15(1):24-6.
16. Ramesh M, Parthasarathi G. Adverse drug reaction reporting: the attitudes and the perceptions of the medical practitioners. Asian Journal of Pharmaceuticals and Clinical Research. April-June 2009; 2 (2):10-14.
17. R.Purushotham Naidu Causality assessment: A brief insight into practices in pharmaceutical industry. Perspect Clin Res. 2013 Oct-Dec; 4(4): 233–236.
18. The use of the WHO-UMC system for standardised case causality assessment. [Last accessed on 2012 Dec 10]. http//www.who-umc.org/Graphics/24734.pdf.
19. Rohilla, Dhulichand; Dureja, Harish Dr., New Drug Approval Process: Regulatory View, Pharmainfo.net, 2010. (Assessed on Sept 5th 2011).
20. Hoffmann E, Fouretier A, Vergne C, et al. (2012). "Pharmacovigilance Regulatory Requirements in Latin America". Pharm Med. 26 (3): 153–164.
21. Rahman SZ, Khan RA (December 2006). "Environmental pharmacology: A new discipline". Indian J. Pharmacol. 38 (4): 229–30. doi:10.4103/0253-7613.27017.
22. https://www.healtheuropa.eu/pharmacovigilance-eudravigilance/88661/ -:~:text=The%20European%20Medicines%20Agency%20
23. Japan Pharmaceutical Manufacturers Association. Pharmaceutical Administration and Regulations in Japan 2002. http://www.jpma.or.jp/ 12english/parj/index.html. Tokyo, Japan: JPMA. Accessed 28 November 2002
24. Health Canada. 2007a. Brief history of drug regulation in Canada [online]: Available from hc-sc.gc.ca/dhp-mps/homologation-licensing/info-renseign/hist-eng.php.
25. Edwards I.R. and Biriell C. (2007). WHO Programme - Global Monitoring. In: Pharmacovigilance, Mann R.D., Andrews E.B., Eds. John Wiley & Sons, Ltd.: 151-166.
26. Gupta Y. K. (2010). Pharmacovigilance Programme for India.July2010.
27. Duvvuru Ashok Kumar, Languluri Reddenna, Shaik Ayub Basha. Pharmacovigilance Programme of India.
28. https://www.slideshare.net/bdvfgbdhg/central-drug-standard-control-organisation
29. Vivek S. Dave. Current Trends in Pharmacovigilance. Journal of Pharmacovigilance. Dave, J Pharmacovigilance 2013, 1:2DOI: 10.4172/2329-6887. 1000e104.