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REVIEW ARTICLE

Pharmacovigilance - An Overview in a Pharmacist Perspective

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ABSTRACT:

The Pharmacovigilance is the scientific activity of identification, evaluation, understanding, and prevention of adverse drugs reactions and other medication-related issues. An "adverse drug reaction" is any hazard, unwanted effect of a drug, which occurs in a normal dose used in humans for prophylaxis, diagnosis, therapy or modification of physiological functions. In India Pharmacovigilance was started in 1986 but it is failed due to various reasons. The Present Pharmacovigilance Program initiated in 2010 and progressing successfully. The aim of the Pharmacovigilance program of India is establishing Indian ADR reporting system and to create own ADR database for the country. The under-reporting of ADR is an important challenge for PVPI to overcome these Technological advancements should be involved. The pharmacist is an integral part of PVPI because of their role in the various levels of the Health care system and immense knowledge about drugs. Hospital pharmacist plays a significant role since most serious ADR occurs in Hospitals. The tremendous growth of Pharmaceutical Industries and Clinical research leads to expansion of PVPI in India. In future PVPI planned to introduce a course on Pharmacovigilance to medical and paramedical students to promote drug safety. The Pharmacovigilance program helps to promote ADR reporting and educate Health care professionals to assure patient confidence in Health care system.

KEYWORDS: Pharmacovigilance, Adverse drug reaction, PvPI, Clinical research, Health-care system.

INTRODUCTION:

The Pharmacovigilance is the scientific activity of identification, evaluation, understanding, and prevention of adverse drugs reactions and other medication-related issues[1]. An "adverse drug reaction" is any hazard, unwanted effect of a drug, which occurs in a dose used in humans for prophylaxis, diagnosis, therapy or modification of physiological functions.[2] No drug is free from ADR but many ADR is preventable and the harm to the patient can be minimized by appropriate care [3]. The term Pharmacovigilance is derived from the word 'pharmakon' means 'medication' in Greek and 'vigilare' means 'to keep alert' in Latin[4].

The Pharmacovigilance includes reporting ADR of herbals medicines, blood products, medical devices, vaccines; it also focuses on safety issues of drug and thereby minimizes harm to patients[5]. Every drug has its own side effects so it is important to assess the drug based on both therapeutic and adverse effects to give ideal drug therapy and to reduce the harm to the patient. The Pharmacovigilance is not only reporting of an Adverse event of drug and it also consists of reporting various issues like poor quality of medicine, medication error, irrational use of the drugs, drug-drug and drug-food interaction[3]. Both clinical trials and post-marketing surveillance are vital for pharmacovigilance. Clinical research is a crucial and inseparable part of the pharmacovigilance[6]. It is mandatory to report every adverse event of drugs in each phase of the clinical trial. Pharmacovigilance encourages safety and quality assurance of drugs products. It is an excellent tool to ensure the safety of patients.

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NEED FOR PHARMACOVIGILANCE:[7,8]:

The Importance of Pharmacovigilance

- *In vivo* drug testing or Drug experimentation on animal provides inadequate evidence about the safety of a drug in Human use.
- Clinical trials provide limited drug safety data as trails are carried out in a small population that is highly screened for specific and selected age, gender, indications, and disease during a short time span.
- Lack of clinical drug safety information for a special population like Pediatrics, Geriatric and, Pregnant.
- To monitor rare, serious adverse effect, and toxicity of drugs.
- The difference in prescribing pattern among prescribers.
- Adulteration in medications.
- Intraindividual and Interindividual variability of drug plasma concentration among populations.
- Patients can be protected from many unwanted and preventable ADRs.
- To lower the Health-care cost and avoid economic burden on the patients.
- To endorse rational use of drugs and adherence of medications.

The Need for Pharmacovigilance in India[9,10]:

- India is the second largest populated country in the word.
- India has a more different and complex ethnic group of people.
- Prevalence of Malnutrition and Vitamin Deficiencies among Indian population.
- A Sudden increase in clinical trials due to its massive population.
- The pharmaceutical and Health care industries are growing in a tremendous rate.
- India is the largest producer of generic drugs and nearly 80% of Antiretroviral drugs.
- An alarming increase in use of OTC, Traditional and Herbal drugs and misuse of medication.

In Mumbai 6.9 % of hospital admissions and 0.85% fatality occurs due to ADR[11]. The Pharmacovigilance program helps to promote ADR reporting and educate Health care professionals to assure patient confidence in Health care system[12]. There is an immense need for Pharmacovigilance program in India to watch adverse events of drugs.

HISTORY OF PHARMACOVIGILANCE OF INDIA:

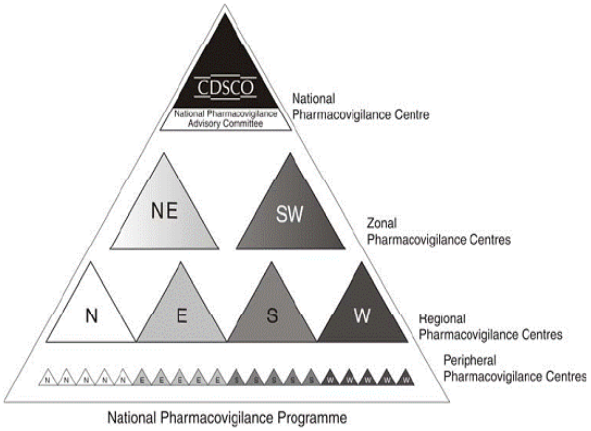
In India, Pharmacovigilance initiated in 1986, this program consists of 12 ADR monitoring centers, but later there was no improvement and special attention given to the Pharmacovigilance activity. In 1997, India joined the WHO ADR Monitoring Program organized at Upscale-Sweden. This support does not improve enough Pharmacovigilance activity improvement and the attempt became a failure. Later the World Bank and WHO collaborate to fund the National Pharmacovigilance program in India[9]. To initiate Pharmacovigilance activity in India which was monitored by the National Pharmacovigilance Advisory Committee based on CDCSO and two Zonal centers established in Mumbai and Delhi to collect information all over the country and send it to WHO AD Monitoring Centre, Uppsala-Sweden[3]. This attempt was unsuccessful to promote pharmacovigilance in India[13].

PRESENT PHARMACOVIGILANCE PROGRAM:

In 2010, the government of India started the PV Program in India (PvPI) a nationwide Pharmacovigilance program under the Central Drugs Standard Control Organization (CDSCO), Directorate General of Health Services by the guidance of Ministry of Health and Family Welfare of India (MOHFW) collaborated with the Indian Pharmacopoeia Commission program[3]. All India Institutes of Medical Sciences (AIIMS), New Delhi is constituted as National Coordinating Centre (NCC) and 22 ADR monitoring centers (AMC) were established. Later in 2011 Indian Pharmacopoeia Commission (IPC), is selected as a National Coordination Centre (NCC) for the Pharmacovigilance Program of India (PvPI)[15].

ORGANISATION AND STRUCTURE:

The Pharmacovigilance Program of India (PvPI) has progressed impressively over the most recent years. It creates a nationwide system for patient safety reporting. There are 250 functioning Adverse Drug Monitoring centers in the country as part of the Pharmacovigilance Program of India[14]. The AMC collects the Individual Case Safety Reports (ICSRs) and gathers more information about suspected drug and its adverse events. They evaluate and report it to regulatory agencies under Pharmacovigilance program. The Approved Government and Private Hospitals, Medical colleges, Independent institution can work as ADR Monitoring centers in India. AMCs are important for active reporting of ADRs to NCC and collect the ADR data to record in the WHO Vigiflow software[16].



(Referred from https://www.aiims.edu/en/national-introduction.html?id=166)

The Various Levels of Pharmacovigilance centers established in India, according to the Pharmacovigilance Program in India (PVPI) are National Pharmacovigilance Center (NPC) at the CDSCO, New Delhi. Two zonal Pharmacovigilance centers in Mumbai for South-West zone, New Delhi for North-East Zone. There are five regional Pharmacovigilance centers at Kolkata, Mumbai, Nagpur, Delhi, Pudhucherry and 30 peripheral pharmacovigilance centers in India. The Pharmacovigilance Programme of India will be administered and monitored by the Steering Committee and Strategic Advisory Committee. The NCC functions under steering committee [18]. The Members of steering committee are:[19]

- Chairman, AIIMS, New Delhi, (ex officio)
- Assistant Drugs Controller, New Drugs (India) act as Member Secretary ,
- Drugs Controller General (India), (ex officio)
- Head of Department, Pharmacology in AIIMS, (ex officio)
- Scientific Director of India Pharmacopoeia Commission, Nominee of Director General, ICMR, (ex officio)
- Nominee of Vice Chancellor of Medical/Pharmacy University, (ex officio)

Technical support will be provided by the following committees:[14]

- Signal Review Panel: It consists of Scientist and Clinicians to detect and evaluate signal from the submitted ICSRs to create promising and important examined Standard report for Drug safety.
- Core Training Panel: It organizes zone wise Training program, module and establishes training centers.
- Quality Review Panel: it reviews submitted forms and reports and gives the recommendation to Pharmacovigilance administration Committees

GOALS:[14],[16]

- To start and develop pharmacovigilance activity in India
- To recruit and employ all approved Medical colleges and Hospitals into the Pharmacovigilance system.
- To engage health care professionals in reporting of ADR.
- Collection and Documentation of ADR report, Individual Case Safety Reports, and Drug safety data.
- To expand the Pharmacovigilance program to all Health care centers India
- To develop and implement an electronic reporting system
- To develop a reporting culture among health care professionals
- To make ADR reporting mandatory for health care professionals

Reporting ADR:[16, 17,18]

ADR is unpreventable part of the Drug therapy but ADR reporting is essential to prevent harm and ensure protection to the patient in the future. A good pharmacovigilance practice can improve ADR reporting in India. This will be not only increase reporting of ADR but also reduce the harm and health care cost to the patient.

Eligibility Persons for reporting ADR:

All health care professionals like Doctors, Pharmacists, and Nurses, etc., Manufacturers of a medicinal product, Health care centers and consumers can report [14]

ADRs that can be reported are as follows: [14]

- Serious adverse drug reactions like death, life-threatening, hospitalization (short or extended), disability (acute or permanent), congenital abnormalities.
- Report non-serious, known or unknown, frequent or rare adverse drug reactions
- For new drugs report all suspected reactions
- Report adverse drug reactions for already marketed, established or well-known drugs
- Report all suspected ADRs associated with drug-drug, drug-food or drug-food supplements
- Report it in case of drug abuse, irrational drug use, overdose or medication error
- Report for ADRs are associated with the withdrawal of drugs
- Report when there is a lack of efficacy or when suspected pharmaceutical defects are observed.
- Report for OTC, Herbal and Traditional drugs.

Information mandatory for ADR reporting:[14]
Patient name, age, gender, onset of reaction, reaction term, date of the onset of reaction, suspected medication, concomitant drugs used and reporter information.

MODES OF REPORTING ADR:[3,18]
There are 2 types ADR reporting form available in India. They are suspected ADR reporting forms for Health care professionals and consumers. The consumer ADR reporting form made available in 10 local native languages accessible in the following website (www.cdsco.nic.in) and (http://www.ipc.gov.in/PvPI/adr.html)

The other way for reporting ADR and contact NCC are:

- Email: pvpi.ipcindia@gmail.com
- Toll-free number: **1800-180-3024** active on weekdays 9 am to 5 pm
- Mobile app: ADR PVPI available in google play store (launched by NSCB Medical College, Jabalpur in 2015 and updated in 2017)
- PVPI also communicated through social media like
- LinkedIn (NCC PvPI)
- WhatsApp (7042343309)
- Facebook (Ncc-PvPI Ipc)
- Twitter (@IPCNCCPvPI)

What happens to the submitted ADR form:[20,21]

- Completed ADR reporting form should be submitted to nearby AMC or directly to NCC
- The information is gathered from the ADR reporting form and maintained confidentiality.
- The causality of reported ADR will be assessed by using WHO-UMC causality assessment scale.
- The Report should be forwarded to the NCC ADR database through WHO vigiflow software.
- Then the collected data is assessed and uploaded to the Global Pharmacovigilance Database managed by WHO Uppsala Monitoring Centre in Sweden.
- The reports are regularly analyzed by the NCC-PvPI to assess for the risk-benefit proportion of drugs.
- The Signal Review Panel of PvPI evaluate the report and give recommendation if required to create a new signal. (‘A signal represent ‘reported information have conceivable evidence to prove that drug has an adverse event .’)
- The data obtained from ADR report forms are utilized for creating and strengthening Signal, Handling Risk, Regulation of Drugs, Education purpose, and benefits.

REPORTING FOR OTHER MEDICAL PRODUCTS:

- **Adverse Event Following Immunization (AEFI):**

In India, AEFI was established in 2010 under Universal Immunization program collaboration with IPC to safeguard the life of neonates, children, and pregnant women. Like other medical products vaccines also have some potential risk and adverse effects. AEFI surveillance program monitor immunization program to ensure safe vaccination and to maintain people’s faith in the Immunization program[14].

AEFI report form is available in website http://www.ipc.gov.in/PvPI/adr.html

- **REPORTING FOR BIOLOGICALS:**

In 2012, The Haemovigilance Program of India (HvPI) was started under PVPI for monitoring and reporting the adverse event of Biological products. The National Institute of Biological (NIB) act as NCC for HvPI is to watch and investigate the unfavorable and hazardous effect that occurs due to blood transfusion and other blood products[14].

Transfusion Reaction Reporting Form (TRRF) For Blood and Blood Components and Plasma Products is available in (http://nib.gov.in/Haemovigilance/TRRF_Form.pdf)

- **REPORTING FOR MEDICAL DEVICES:**

Materiovigilance Program of India (MvPI) was launched in 2015 to detect the adverse and harmful effect of medical devices. The IPC and CDSCO act as regulator and NCC for MVPI. In recent times India became the 4th largest consumer of Medical devices. In 2017 Government of India regulates production and imports of Medical device in India[21].

Medical Device Adverse Event reporting form is available in www.cdsco.nic.in/writereaddata/MDadverseevent.pdf

ROLE OF PHARMACIST:[23,24,25]
The role of Pharmacist is important for Pharmacovigilance due to their extensive knowledge about Drugs. This supports them to understand the nature and characteristics of ADR. Pharmacist expertise in drugs helps to identify suspected drug which causes ADR. Pharmacist surveillance for ADR will benefit Pharmacovigilance and reduces medication error and promotes the rational use of drugs. The important part of a pharmacist in drug safety is early identification of ADR. In a Health-care system, pharmacist may act serve as a backbone in reducing the incidence of ADR. In India, Pharmacist is not well established like developed

countries and their role is limited in the present situation in the Health care system in the current scenario.

The significance of Hospital Pharmacist in Pharmacovigilance is:

- Most of serious ADR occurs in Hospital.
- The complete and quality ADR reports can be obtained from hospital pharmacist.
- Direct engagement with patient and other Health care staffs in the hospital.
- They can monitor safety of drugs prescribed to the patients.
- To educate Hospital staffs about ADR monitoring and reporting.
- To educate Patient about potential ADR of drugs used in treatment.

In the USA, Hospital Pharmacist is a major contributor of Pharmacovigilance. The FDA receives most of the high standard ADR reports from Hospital Pharmacist when compared to other Health care professional.

BARRIERS FOR PVPI:[26,27,28]

Pharmacovigilance is significant for Drug safety and an essential tool to detect ADR of drugs. The various types of barrier are listed below.

SOCIAL BARRIER:

- Lack of involvement by Government to promote Pharmacovigilance activity.
- Poor Funding and Infrastructure
- Less priority to Pharmacovigilance in India.
- Complicated system for reporting ADR
- Low literacy rate in the country

PROFESSIONAL BARRIER:

- An inadequate number of professional staffs in Health-care system.
- Lack of time, Intent and motivation for Health care staffs to report ADR.
- No proper maintenance of Patient records.
- Not empowering other Health care professionals except Physicians.
- The poor prescribing pattern among physicians and not following guidelines properly.
- Lack of Knowledge and Training in ADR reporting among Health-care professionals.
- Fear of Blame and Negative impact on career among Health-care professionals.
- Ignorance of ADR and not considered as serious to report.
- Not mandatory to report ADR.
- Prioritize drug therapy and not monitoring ADR.
- Difficulties in identify the Suspected drugs and recognize the ADR.

PATIENT BARRIERS:

- Lack of Knowledge and awareness about ADR reporting among people.
- Self-medication and using herbal drugs, counterfeit drugs, and traditional medicines.

The above Barriers can increase the risk of ADR in India. The Government plays a critical role in overcoming these barriers by strictly enforcing the rules and regulation for Pharmacovigilance. The training program and modules will increase awareness among Health care professionals and Consumers about Drug safety. The easily approachable and simple reporting methods can increase ADR reporting activity. In 2017 the National Strategic scale up Plan for Pharmacovigilance was started to establish PVPI program in District and rural hospitals and Public Health centers to assist the current Pharmacovigilance program and started a nationwide skills development program on pharmacovigilance for healthcare professionals.[3]

CONCLUSION:

In the current scenario, PVPI attained success in establishing the pharmacovigilance system in our country but still, pharmacovigilance and ADR reporting is not widely spread among the Indian population. The under-reporting of ADR is a major concern for PVPI and it takes various steps to use major advancement in technologies for enhancing Pharmacovigilance activity. In future PVPI has planned to introduce a course on Pharmacovigilance to medical and paramedical students in order to promote drug safety. From past pharmacovigilance program failure, India learned its lesson and has built PVPI in collaboration with Global Pharmacovigilance system. An advertisement about ADR reporting promotes PV activity in India. The tremendous growth of pharmaceutical industries and clinical research lead to expansion of PVPI in India. With the help of private sectors, Indian pharmacovigilance program can achieve good ADR surveillance and ensure drug safety.

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CONFLICT OF INTEREST:

The authors declare no conflict of interest.

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