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Pharmacovigilance in India: Do Not Take a Chill Pill

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ABSTRACT

Pharmacovigilance is also often understood as Drug Safety. For drug safety, Adverse Drug Reaction (ADR) must be monitored throughout the life of the drug, from its development, clinical trials, and post-approval. The discipline of Pharmacovigilance has gained its due importance in India recently in the last 10 to 15 years. The importance of pharmacovigilance increases even more in the pandemic situation. Numerous drugs are being used empirically according to experience and availability to treat Covid-19. The pandemic is an insight to regulate the highly unregulated drug distribution system. The system can be strengthened by training of the human resource, public-private partnership, legislation, communication, research and innovation Pharmacovigilance has witnessed substantial development over the years, yet there is a need for a practical revolutionary roadmap to tackle all the hindrances to fortify its symphonic functioning. The public confidence around the efficiency of Pharmacovigilance will build when people have access to good-quality and safe medicines and a suitable system for the distribution of medicines that have cleared Pharmacovigilance.

Key Words: Pharmacovigilance, Adverse side effects, Covid 19, Challenges, Recommendations, Public health professional

INTRODUCTION

Pharmacovigilance is also often understood as *Drug Security or Drug Safety*. The historical roots of the word "pharmacological vigilance" are pharmacon (Greek for medicine) and viglar (Latin means to watch). The World Health Organization (WHO) outlines"pharmacovigilance" as the science and activities related to detecting, evaluating, understanding, and preventing side effects or any additional problem related to drugs and vaccines.[1]All the medicines, drugs, vaccines, devices, and other related products undergo rigorous testing before the concerned authorities approve them for public use, but drug toxicity is still a relatively common phenomenon.

The clinical trials to test the drug include few sampled individuals for a limited period. However, specific minor adverse reactions are evident only after a certain period of exposure. Once the drug or active substance is approved for the heterogeneous population over a considerably long time, the chances of getting an adverse reaction from it are significantly high. For drug safety, Adverse Drug Reaction (ADR) must be monitored throughout the life of the drug, from its development, clinical trials, and post-approval.

History of Pharmacovigilance

The history of Pharmacovigilance traces its root 173 years back when a young girl (named Hannah Greiner) died on January 29, 1848, after receiving chloroform sedation before removing an infected toe's toenails. [2]Then, in 1937, 107 people died in the United States from a sulfanilamide elixir containing diethyl glycol as a solvent. The solvent was then identified to be the cause of death. As a result, the Federal Food, Drug, and Cosmetic Act was created in 1938. This law aims to renew the public health vigilance system. [2]

'Thalidomide Tragedy':An evident change in the scenario of Pharmacovigilance occurred in 1961, when Dr. McBride, an Australian doctor, detected that the incidence of congenital deformities of babies had amplified significantly (up to 20%) in women who had taken thalidomide through pregnancy for treatment of nausea.[3]This tragedy has highlighted several critical issues regarding the reliability of animal testing, industrial drug company behavior, and the

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importance of post-marketing drug monitoring, causing a change in pharmacovigilance regimen. Automatic reporting of adverse drug reactions has become more systematic and structured.[2]In 1968, the WHO Programme for International Drug Monitoring was inaugurated to ensure transparency around medicines' safety to the public.

Pharmacovigilance in India:

The pharmacovigilance system has recently gained significant importance in India over the last 10 to 15 years. An official ADR monitoring system was established in 1986 under the direction of the Pharmaceutical Controller of India. The National Pharmacovigilance Program was launched in 2005 and was renamed the Indian Pharmacovigilance Program (PvPI) in 2010 to become a robust pharmacovigilance system in India. The mission is to protect the overall health and well-being of the Indian population; by safeguarding the benefits of drugs that offset the risks associated with their use.

Under the Government of India (GoI), the Ministry of Health and Family Welfare (MoHFW) recast PvPIon April 15, 2011. It transferred the National Coordination Centre (NCC) to the Indian Pharmacopoeia Commission (IPC) Ghaziabad from the All India Institute of Medical Sciences (AIIMS), New Delhi.[4] The Central Pharmaceutical Standards Control Organization (CDSCO), the General Directorate of Health Services under the MoHFW, GoI, and the Indian Pharmacopoeia Commission Ghaziabad runs a nationwide pharmacovigilance program. The Indian Pharmacopoeia Committee in Ghaziabad coordinates the program as the National Coordinating Center (NCC). The Center works under the supervision of a steering committee.

All technical issues related to program establishment and implementation, including technical inputs, are handled by the working group that reports to CDSCO for organizational interventions. The Quality Review Committee is responsible for the quality, causality assessment, and completeness of the data. The PvPI Signal Review Panel (SRP) consists of scientists and clinical experts from government and non-governmental, academic institutions and hospitals. This committee analyzes the data reported by various Adverse Reaction Committees (Total 270 across India) and decides which adverse effects need attention and action. [5]

The Programme is supported by the Training panel, whose primary function is to identify training needs, organize national and international training programs, design modules for training. It helps conduct the training for various healthcare professionals and other key stakeholders throughout the year. PvPI also addresses counterfeit drugs, antimicrobial resistance, surveillance during mass vaccinations, and other national programs.[6] In July 2017, WHO bestowed upon India to honor being one of six countries globally as a WHO collaborating Centre for Pharmacovigilance center for Public Health Programme and Regulatory services.

The general activities of PvPI are to collect and manage data related to drug safety. The data is used to discover "signals," information about new or potentially changing safety issues that any drug may cause. Then evaluate the data collected to make decisions on safety issues, proactively manage risks to mitigate associated risks, defend public health, including regulatory actions, communicate and inform stakeholders and the public, and monitor critical results and related processes. [7]

Pharmacovigilance and Covid-19

At present, there is no approved treatment regimen for Covid-19 disease. Numerous drugs are being used empirically according to experience and availability. Hence the role of Pharmacovigilance increases multiple folds under pandemics. Amongst all those drugs used for the treatment of Covid-19, Glucocorticoids have the highest ADR reported.[8] The robust ADR monitoring system allows putting safety checks on the medicines producing severe ADRs.

The scientific community is busy inventing new vaccines to deal with the pandemic. Since more and more vaccine trials develop, inevitably, more complications associated with adverse events and rare side-effects can be seen shortly. PvPI must intervene to ensure the best possible vaccine option with a minor health hazard in such circumstances. One such proven effective measure is the use of digital technologies to optimize ADR reporting in the pandemic time.

The vaccine and drugs used for treatment pose challenges, but the consumption of Over-the-Counter (OTC) drugs and self-medication has exponentially increased during the pandemic.[9] The drugs flowing in the private sector channel escape scrutiny via various regulating authorities, and the pharmacists provide drugs without a medical prescription. The pandemic is an insight to regulate the highly unregulated private sector networking of drugs distribution ADR reporting mechanism both by the pharmacist and the general public.

Role of Public Health Professional in Pharmacovigilance

The country has more than 23 lakh registered health care professionals, including AYSUH and dentists, who can contribute to an extensive database by reporting even a single ADR per year.

All public health programs have a significant component of medical products, procurement, and distribution, with public health professionals and managers. However, the pharmacovigilance arm of the program component is weakest. It should be inherent in every new health program/scheme and

old health programs and schemes.

Some health programs like the Universal Immunization Programme vaccinating children and pregnant females and the National TB Elimination Programme have a robust Adverse Effect Following Immunization (AEFI) / ADR reporting mechanism. For AEFI monitoring in UIP, a whole State level AEFI task force exists. Similar efforts are needed to improve ADR reporting other national health and state health programs. All programs managers should be promoted, trained, motivated, and incentivized to identify, report, and analyze ADRs occurring amongst the beneficiaries of various health programs. They can play an active role in creating awareness about potential ADRs and their reporting in the community through health education and promotion campaigns.

Challenges

The Pharmacovigilance system undergoes many challenges on a global front. The system is well developed in the high-income countries like United States, United Kingdom, and Germany, while the middle- and low-income countries like India are still evolving.[10]Globally, only about 500,000 to 700,000 adverse events are recorded each year. Conversely, low- and middle-income countries, which make up more than sixty-six percent of the world's population, make up a small portion of all ADR data. [11]

India is the world's second most populated country, with over one billion budding drug users. Also, the country caters to more than six thousand licensed drug producers and over 60,000 branded drug preparations.[12]Although the country's participation is minimal in the world's ADR database.It is estimated that around 8% of hospitalizations in India are due to ADR, and 8-19% of hospitalized patients have severe ADR.[13]

The main challenges faced by the system include different regulatory authorities with different forms of ADRs and different timelines for each country. As the system is still evolving, there is a vast regulatory gap due to continuously changing guidelines. Such diverse regulations make compliance a big challenge. Not only this, an enormous global gap exists in the gross reporting of ADR, too, due to a lack of awareness amongst both the health care practitioners and the public. The European-Americanshave been reporting the ADR for ages while the Asian-Africans are still learning.

Over the years, the quality of data reported has improved in its completeness. However, the Programme has not provided the exact incidence of ADRs among different medicines, including allopathic and AYUSH medicines.[5] Both ordinary people and healthcare professionals rely on foreign data and studies. Furthermore, not much research has been conducted in this area.

Self-medication via herbs (owing to the high doctor-patient ratio and accessibility) and other traditional forms of medicines often possess a significant barrier in the drug safety of the third world. Cultural, linguistic diversities, and economic determinants in the eastern countries are also a setback in adequate ADR reporting mechanisms.

There is little knowledge and motivation among practicing and teaching health care professionals, pharmacists, medical and laboratory technicians, and the layman about the importance of Pharmacovigilance. The Public Health Services lack laboratory services to diagnose even severe ADRs.

DISCUSSION

Few perspectives on improving the system are on following domains:

Training: The Pharmacovigilance System can be included in Under and Post Graduate Medical, AYUSH, and Para-Medical Courses. A comprehensive training needs to be initiated that envelope all aspects of Pharmacovigilance both in practice and clinical research.

Legislation: Pharmacovigilance reporting should be made mandatory and binding for medical colleges, Private Hospitals, and Clinics to enhance the reporting.

Human Resource: Motivated leaders and well-trained team members are the pillars of the success of any program. Healthcare professionals, including physicians, nurses, and pharmacists, are the backbone of the healthcare system, contributing to patient safety. There is a mandate of assigning responsibilities of Pharmacovigilance on Nodal Officer in each medical college, but no such mandate exists for private hospitals, diagnostic centers, and clinics. The private sector health care industry caters to sixty-six percent of the total Indian population [14]; still, there is no legislative compulsion on the private players to recruit any Pharmacovigilance Cell/ Officer or Nodal officer.

Research and Innovation: The European Union introduced an inverted black triangle on medicinal products subject to additional monitoring to improve ADR reporting. The patients and healthcare professionals can quickly identify these products visualizing the black symbol. The supplementary text inside the drug packet emboldens the consumers to report any unexpected and untoward adverse reactions through national reporting systems. [7]A similar initiative can be implemented in the Indian system.

Studies such as the role of drug alerts have influenced the decision of Health care providers in improving patient safety; thereby, translating evidence into actions should be commissioned.

Also, lessons learned from the pandemic, paperless reporting should be expanded. Once the patients' data is collected us-

ing Electronic Health/Medical Records, reporting from OPD and IPD facilities enhances spontaneously. Automated, user-friendly IT systems can incorporate the revolutionary change for ADR reporting.

Communication: Although the PvPI-IPC regularly issues drug alerts to the AMCs, this knowledge is seldom disseminated to the public. An effective IEC/Media Cell should be established under the PvPI, whose functions would be to issue public advisory regarding ADR, risk communication, and fight fake news circulating in print and social media.

Partnership & Collaboration: The Public-Private Partnership model must be incorporated in the ADR reporting system involving critical stakeholders of pharmaceutical companies and the public sector. In India, the medicine distribution system is mainly informal. The pharmacist largely influences the population may it be the consumption of OTC drugs or otherwise. Hence the role of the pharmacist in the Indian scenario is vital. The pharmacist can advocate people to report ADR and report the ADR on behalf of patients if trained, motivated, and incentivized.

Public Participation: In pill-popping countries like India, there is a rising population of "Google doctor" patients who investigate, diagnose, and treat themselves using internet search engines. They rarely use formal tax drug interaction reporting systems but actively use online platforms to research and report potential adverse drug reactions. The consumer forums are a potential platform for collecting vital data on ADRs, currently unexplored and unutilized.

Involving patient groups in dissemination meetings or public hearing helps bridge the gap between doctors and patients, improve medical knowledge, increase ADR reporting and assist decision making.

CONCLUSION

Pharmacovigilance has improved significantly over the years, but a practical and revolutionary roadmap is needed to remove all barriers to improving its symphonic performance. As more and further clinical drug trials and other clinical research activities are being conducted in countries like India, there is a prerequisite to understanding the importance of Pharmacovigilance as soon as possible. The public confidence around the efficiency of Pharmacovigilance builds when people have access to good-quality and safe medicines and a suitable system for the distribution of medicines that have cleared Pharmacovigilance. With the augmentation of Pharmacovigilance, the pharmaceutical industry is sure to witness a paradigm shift towards safe and reliable medical care for all.

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