Evaluating Drug Safety in The Era of Covid-19: A Review of Pharmacovigilance Practices

Alla Geethika Pravanya[1], Pallagolla Harika[2], Harshitha Nagothu[3]
[1,2]*Student, Doctor of Pharmacy (Pharm.D)*
[3]*Student, Master of Pharmacy (M.Pharm)*

Abstract-The COVID-19 pandemic has led to the rapid development and widespread use of various medications to treat and prevent the virus. As with any new drug, it is important to carefully assess the safety and effectiveness of the treatments. This review aims to examine pharmacovigilance practices for evaluating drug safety in the context of COVID-19. We begin by defining pharmacovigilance, its functions and importance during the pandemic era. This report also discusses about various types of data sources used in pharmacovigilance, including spontaneous reporting systems, clinical trials, and observational studies. Finally, conclude with the challenges and limitations of pharmacovigilance during the COVID-19 pandemic and suggested strategies for improving drug safety monitoring in this rapidly evolving situation. Overall, this article highlights the crucial role of pharmacovigilance in ensuring safe and effective use of medications in the fight against COVID-19.

Keywords: COVID-19, pharmacovigilance, drug safety assessment.

INTRODUCTION TO COVID-19

The COVID-19 pandemic heightened global awareness of the profound, unprecedented threat posed by the SARS-CoV-2 virus (Severe Acute Respiratory Syndrome Coronavirus) and its evolving genomic variations, threatening individual health as well as global business relationships and dynamics. [1] COVID-19, also known as the coronavirus disease, is a highly infectious respiratory illness caused by the SARS-CoV-2 virus. It was first identified in Wuhan, China, in December 2019 and has become a global pandemic. To combat the spread of the virus and treat infected individuals, numerous medications and vaccines have been developed and are being used globally. It is therefore critical to carefully evaluate the safety and effectiveness of these treatments to ensure that they are used appropriately and effectively. [2]

The virus is highly contagious and can be transmitted from person to person through respiratory droplets produced when an infected person talks, coughs, or sneezes. Symptoms of COVID-19 can range from mild to severe and may include ageusia, anosmia, fever, nausea, diarrhea, cough, body aches, fatigue, shortness of breath, severe respiratory illness and death. Governments around the world have implemented various measures such as lockdown, social distancing, and wearing masks to slow the spread of the virus. Vaccines have also been developed and are being distributed to prevent further transmission of the virus.[2]

PHARMACOVIGILANCE IN RELATION TO COVID-19

Generally, Pharmacovigilance is defined as the science and activities that are related to the detection, assessment, understanding, prevention, and communication of adverse effects or any other medicine-related problem to the appropriate stakeholders. The major categories of functions that are included in the PV system are as follows:
(1) Case management (collecting adverse events, processing of a case, Individual Case Safety Report [ICSR] and SUSAR (Suspected Unexpected Serious Adverse Reaction) reporting to regulatory authorities (RA), Reporting and evaluation of aggregate cases);
(2) Signal management (it involves a series of steps for identifying, evaluating, and communicating potential safety concerns related to medications)
(3) Benefit-risk management.[1]
The pandemic had elicited challenges for the whole healthcare sector. Pharmacovigilance (PV) methods are also hampered due to the COVID-19 pandemic. During COVID-19, patients were administered with various repurposed and newer drugs, which could

have led to the occurrence of numerous ADRs. ADR reporting is very critical to ensure the short- and long-term safety of the pharmacotherapy administered to COVID-19 patients. As a result, it is critical for healthcare professionals and the pharmacovigilance team to bond together and collaborate to overcome the barriers for reporting ADRs by developing and implementing various new ideas. [3]

CONSEQUENCES OF COVID -19 IN PHARMACOVIGILANCE AND MEDICATION SAFETY

The impact of COVID-19 pandemic has been catastrophic and has demanded that the pharmacovigilance (PV) field innovate by developing new and more effective ways of gathering and utilizing drug safety information. COVID-19 had a greater degree of impact on different PV areas like ICSR processing, aggregate review, signal management, and risk management. [1] These impacts demanded PV centers to adapt their organization and workflow according to the needs of the pandemic. For pharmacoepidemiologic surveillance of COVID-19 drugs, various active PV approaches were implemented for better coverage. The implementation of an effective communication strategy raised awareness about the importance of reporting suspected adverse reactions to COVID-19 vaccines and other drugs.[4] Various lessons that are learned due to COVID-19 on pharmacovigilance include:

Electronic reporting: usage of electronic or paperless reporting of ADRs and continuing automated technologies at all levels of pharmacovigilance (focusing mostly on ICSR management).

Virtual Meetings: Employing virtual meeting formats as the primary source of communication for data collection, monitoring, and follow-ups. Conducting webinars for healthcare professionals to keep them motivated and updated on drug safety and pharmacovigilance.

Planning Models: COVID-19 urged the development of redundancy and fallback planning models to attenuate the effects of global risks like pandemics and wars.

Automated Systems for A Responsive and Robust Intelligence Process: Automation dramatically reduces the risk of errors caused by humans during arduous work situations such as pandemics. These systems help with regulatory intelligence maintenance, a rapid change-implementation process, and a robust system to enter rule-based decisions that ensure compliance and quality.

Establishment of a centralized system: A system that performs automated reporting assessment, supports generating and prioritizing tasks, prepares submission packages, and is capable of sending communications to various teams. [1] [3]

NEED FOR PHARMACOVIGILANCE DURING COVID -19

Pharmacovigilance is essential for ensuring that the treatments being administered to COVID-19 patients are safe. Despite the fact that many treatments are being used and studied, we still lack solid evidence to answer issues about the efficacy and safety of many medication candidates given in the pandemic's quick drug discovery process. It would be challenging to guarantee the short- and long-term safety of these medicines if we solely focus on the efficacy of the specific experimental candidate, given the urgent need for a viable treatment or vaccine against COVID-19.

Numerous medications presently in the market are being repurposed for the treatment of COVID-19. Repurposed medications used in the treatment of COVID-19 are antimalarials like hydroxychloroquine (HCQ), antivirals like oseltamivir, lopinavir/ritonavir, remdesivir, and favipiravir, antiprotozoals like ivermectin, immunomodulators like corticosteroids, antibiotics like doxycycline, azithromycin and monoclonal antibodies like tocilizumab.

It is critical to promptly and accurately record, report all adverse events to the pharmacovigilance database. This database would in turn launch a timely review of reported data and signal generation, or crucial safety data that HCPs and prescribers are desperately in need of, in order to gather and pool sufficient information regarding the efficacy and ADRs of COVID-19 therapies or drugs.

To aid healthcare professionals (HCPs) in making informed decisions about the use of certain therapies for COVID-19, the World Health Organization Collaborating Centre for International Drug Monitoring and the Uppsala Monitoring Center have published reports of suspected adverse drug reactions (ADRs) that have been reported to VigiBase, a database of ADR information. These reports can help

HCPs exercise caution and properly administer these therapies. Currently, VigiLyze is also utilized to quickly view and analyze the safety information for medications used in COVID-19. Drug safety for SARS-CoV-2 patients is dependent on ensuring and facilitating the collection of quality data from adverse event reports.[3]

NOVEL THERAPEUTIC APPROACHES AGAINST COVID-19 AND PATIENT SAFETY

So far, several treatment strategies have been investigated in numerous nations to either prevent or treat the SARS-CoV-2 infection and overcome its consequences. The most popular strategy has been "drug repurposing" to look at medications currently in the market with recognized/approved uses for various disorders.

Drugs employed in the field of antiviral medicines diminish the replicating and infectious ability of SARS-CoV-2, and immunomodulatory therapies lower the immune system's exaggerated inflammatory response to SARS-CoV-2 infection, have received special attention. Only dexamethasone and remdesivir have currently been authorized for use in treating COVID-19 patients. In parallel, an enormous effort has been made to create an effective vaccine to lower the risk of infection and serious illness. Four COVID-19 vaccines have received approval until the end of April 2021; these vaccines cause the S protein of the SARS-CoV-2 to express, eliciting an immune response. The mRNA and viral vector vaccines have been widely studied in COVID-19, among the several potential strategies.[4]

An in-depth investigation of the structure and pathophysiology of COVID-19 is being conducted in order to find therapeutic drugs that are effective against the SARS-CoV-2 infection.[5] Two categories exist for therapeutic approaches to COVID-19:

1. Virus-based therapy
2. Host-based therapy

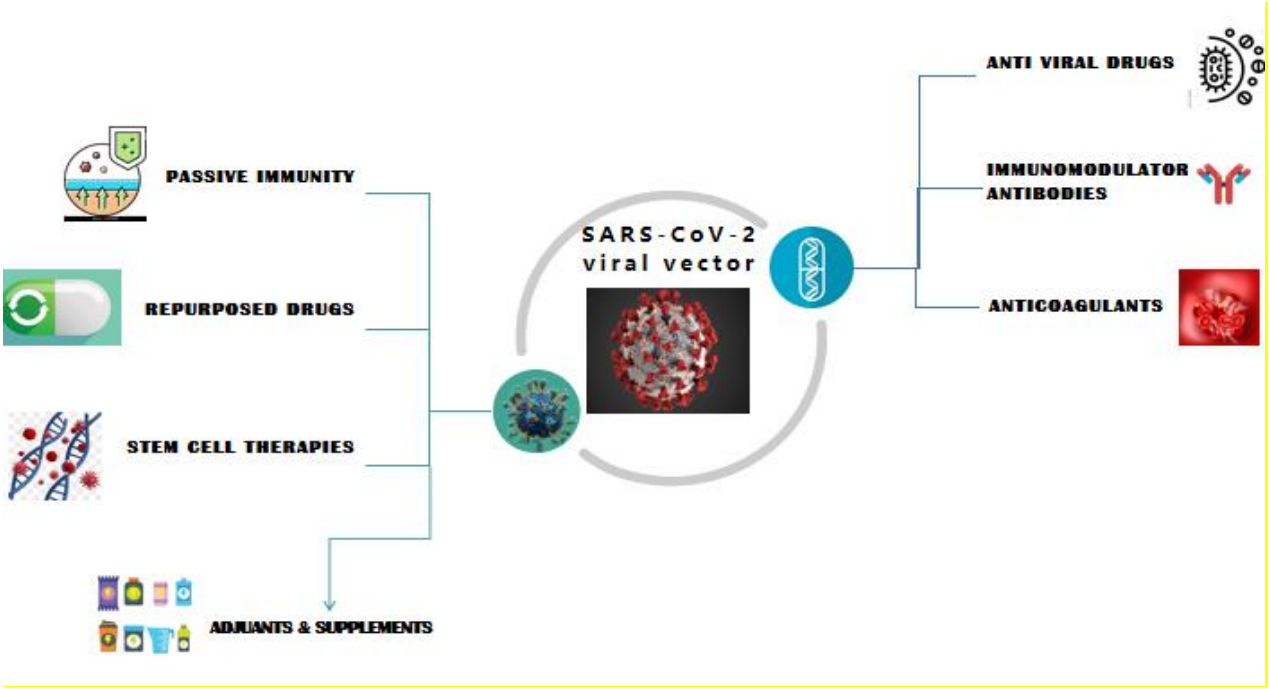

Figure 1: Novel therapeutic approaches to SARS-CoV-2 infection

COVID-19 VS DRUG SAFETY CHALLENGES

Currently, the COVID-19 pandemic has had a negative impact on pharmacovigilance activities. The regular contact between patients and healthcare professionals (HCPs) or residents has significantly decreased as a result of the virus's high infectivity. It has been challenging for the AMCs to submit the ADRs at the same rate and volume due to the lockdown and reduced staff. As a result, it becomes the collective obligation of the HCPs to ensure adequate ADR acquisition, collection, reporting, and

causality assessment in the AMCs. Timely examination of ADR reports and accurate reporting of adverse events will aid in the identification of signals and the creation of many meaningful safety profiles for the tested medicines.

Pharmacovigilance centers are facing certain uncommon difficulties as a result of the COVID-19 epidemic. For instance, when we are presented with a new therapeutic indication for which there is very little information, it is rather difficult to handle drug safety risks, even for medications already in use. The pandemic necessitates prompt actions, which call for expedited safety issue detection, processing, and reporting. This necessity for fast-tracking is particularly problematic because pharmacovigilance centers are overworked due to the significant increase in reports (especially those pertaining to COVID-19 vaccinations).

Furthermore, the COVID-19 pandemic has resulted in a significant increase in false information and fake news. The quick dissemination of false information regarding the efficacy of vaccinations and other COVID-19 treatments has a detrimental effect on the population's adherence to treatment regimens, jeopardizing, for instance, the development of group immunity. Pharmacovigilance must be methodologically rigorous in order to know how to address this concurrent issue using the most up-to-date scientific data.[4][3]

These difficulties forced pharmacovigilance centers to adjust and reorganize, in order to put into practice strategies due to increase in the amount of data that was available regarding the effectiveness and adverse event rates (AERs) of drugs used to prevent or treat COVID-19. Additionally, the exponential rise of ADRs confirms the necessity of giving the work of pharmacovigilance centers top priority.

Additionally, it is imperative to focus on risk communication since the value of all of our pharmacovigilance initiatives will be demonstrated by our capacity to disseminate applicable guidance for the safe use of medications. Overall, the data acquired by COVID-19 pharmacovigilance will help counter false information. Pharmacovigilance reports do, in fact, include the most recent data available from studies utilizing actual data that is methodologically sound and subjected to peer review to provide pertinent assistance for healthcare authorities.[4]

Criteria for drug safety management during the COVID-19 pandemic

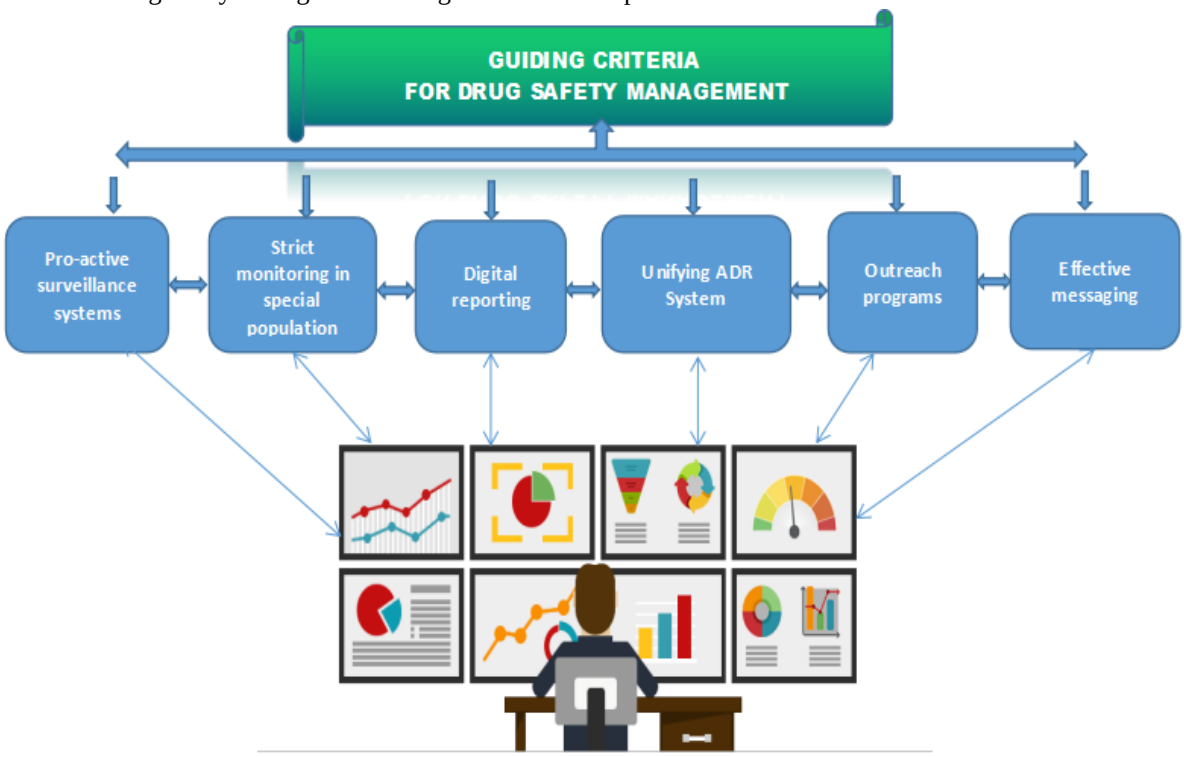

Figure 2: Guiding Axes for Drug Safety Management During the COVID-19 Pandemic

During the COVID-19 pandemic, there are several guiding axes that can be used to ensure the safety of drugs, particularly in regards to pharmacovigilance and the drug safety report assessment. These include [4]

1. Ensuring the timely reporting of adverse drug reactions. This can be achieved by encouraging healthcare providers and patients to report any adverse reactions they experience after taking a drug, and by providing clear guidance on how to report these reactions.
2. Carefully evaluate all drug safety reports. This can be done by establishing clear criteria for the evaluation of drug safety reports, and by using these criteria to thoroughly assess each report to determine its potential impact on the safety of the drug in question.
3. Sharing safety information with relevant stakeholders. This can be done by regularly sharing drug safety information with regulatory agencies, healthcare providers, and patients so that they are aware of any potential risks associated with the use of a particular drug.
4. Taking an appropriate action based on safety information. This can involve a range of actions, such as issuing safety alerts, updating drug labeling, or restricting the use of a particular drug.

Overall, the goal of pharmacovigilance and the assessment of drug safety reports during the COVID-19 pandemic is to ensure that patients have access to accurate and up-to-date information about the safety of the drugs they are taking so that they can make informed decisions about their treatment. This can help to minimize the risk of adverse reactions and improve the overall response to the pandemic.

1. Drug surveillance programs

During the COVID-19 pandemic, active drug monitoring programs played an important role in pharmacovigilance and the assessment of drug safety reports. These programs involve the systematic and ongoing monitoring of drugs, typically through the usage of databases or other information sources, to identify any potential safety concerns. [6]

In the context of COVID-19, active drug monitoring programs can be used to identify any adverse reactions or other safety concerns related to the use of drugs for the treatment of the virus. This information can then be used to inform the assessment of drug safety reports and to take appropriate action to protect the safety of patients.

For example, if an active drug monitoring program identifies an increased number of adverse reactions to a particular drug, this information can be used to evaluate the safety of the drug and determine if any additional action is needed, such as issuing a safety alert or restricting its use.

Overall, active drug monitoring programs can help in improving the safety of drugs used in the treatment of COVID-19 by providing timely and accurate information on any potential safety concerns.

2. Intensive monitoring in special populations

During the COVID-19 pandemic, intensive monitoring of vulnerable population was an important aspect of pharmacovigilance and the evaluation of drug safety reports. Special population are the groups of people who may be at increased risk of adverse reactions related to drugs due to factors such as their age, gender, underlying medical conditions, or other characteristics.[7]

In the context of COVID-19, intensive monitoring in special population can assist in identifying any safety concerns related to drug use in these population. This information can then be used to inform the assessment of drug safety reports and to take appropriate action to protect the safety of these population.

For example, if an intensive monitoring program identifies an increased number of adverse reactions to a particular drug in elderly patients, this information can be used to evaluate the safety of the drug in this population and to determine if any additional action is needed, such as issuing a safety alert or restricting its use in this group of patients.

Overall, intensive monitoring in special population can help to improve the safety of drugs used in the treatment of COVID-19 by providing timely and accurate information on any potential safety concerns in these groups of people. This can help to minimize the risk of adverse reactions and improve the overall response to the pandemic.

3. Electronic reporting

During the Covid-19 pandemic, pharmacovigilance reporting was critical in the evaluation of medication safety data. With many people using many drugs to maintain their health, it is critical to have a system in place to swiftly and efficiently monitor for possible safety risks.[8][4]

Electronic reporting provides for more efficient and accurate tracking of adverse medication responses and other drug safety concerns which can assist healthcare practitioners in making judgments regarding the pharmaceuticals they prescribe, ensuring that the patients receive the safest and most effective therapies. Furthermore, electronic reporting can assist healthcare practitioners and regulatory bodies in swiftly identifying any safety concerns with Covid-19 medicines. This can help guarantee that patients and healthcare practitioners get the most up-to-date information on the safety of these drugs.

Overall, electronic reporting in pharmacovigilance was critical in preserving patient safety throughout the COVID-19 outbreak. It enables more efficient and precise tracking of medication safety data and can assist prescribers in making treatment decisions.

4. Integrative ADRs system

A pharmacovigilance system that integrates diverse data sources to offer a more comprehensive perspective on drug safety is known as an integrative ADRs (adverse drug reactions) system. Source of data can be from clinical trials, post-marketing surveillance, and spontaneous reporting by healthcare providers and patients.

An integrated ADRs approach can be especially beneficial for assessing medication safety data in the context of the COVID-19 pandemic. Usage of multiple drugs by patients to maintain their health has made it critical to have a system in place that can identify possible safety risks promptly and effectively.[9]

Ultimately, during the COVID-19 pandemic, an integrated ADRs system can be a beneficial tool for assessing medication safety complaints.

5. Awareness campaigns

Awareness campaigns can be an effective tool for promoting pharmacovigilance and the importance of reporting adverse drug reactions (ADRs) during the Covid-19 pandemic. These campaigns can educate the public and healthcare providers about the importance of reporting ADRs and the role that pharmacovigilance plays in ensuring the safety of medications. [10]

Awareness campaigns can be particularly important during the Covid-19 pandemic, as many people are taking multiple medications to manage their health. This increases the potential for adverse drug reactions and makes it even more important to have a robust pharmacovigilance system in place.

Awareness campaigns can take many forms, including public service announcements, social media campaigns, and informational materials distributed to healthcare providers and patients. Hence, awareness campaigns can play a valuable role in promoting pharmacovigilance and the assessment of drug safety reports during the COVID-19 pandemic. By educating the public and healthcare providers about the importance of reporting ADRs, these campaigns can help to ensure patient safety and the effectiveness of the medications they are taking.

6. Effective communication

Effective communication is essential in the field of pharmacovigilance, as it helps to ensure the safety of drugs. There are several key components to effective communication in pharmacovigilance and the assessment of drug safety reports. These include:

Clear and concise language: It is important to use language that is easy to understand and free of jargon or technical terms. This will help to ensure that the information is accurately conveyed and can be easily understood by all stakeholders.[11]

Thorough and accurate reporting: Drug safety reports should be detailed and accurate, providing all relevant information about the adverse reaction or safety concern. This will help to ensure that the information is properly assessed and acted upon.

Timely reporting: Timely reporting is crucial in pharmacovigilance, as it allows for timely intervention and can help prevent further harm. Drug safety reports should be submitted as soon as possible after an adverse reaction or safety concern is identified.

Sharing of information: Effective communication in pharmacovigilance also involves the sharing of information with relevant stakeholders, such as healthcare providers, regulatory agencies, and other parties involved in the assessment of drug safety. This can be done through a variety of channels, such as meetings, conferences, and online platforms. Overall, effective communication is essential in pharmacovigilance and the assessment of drug safety reports. It helps to ensure the timely and accurate reporting of safety concerns and enables the effective sharing of this information with relevant stakeholders.

This, in turn, helps to protect the safety of patients and the general public.

CONCLUSION

The COVID-19 pandemic has highlighted the importance of effective pharmacovigilance practices in ensuring the safety of drugs. The rapid development and widespread use of new drugs and treatments for COVID-19 have put a spotlight on the need for rigorous monitoring and evaluation of their safety and effectiveness. Several challenges have been raised in the evaluation of drug safety during the pandemic, including the need for rapid development and approval of drugs, the potential for increased adverse drug reactions due to the use of multiple medications, and the difficulty in conducting traditional clinical trials.

To address these challenges, regulatory agencies and pharmaceutical companies have implemented a range of pharmacovigilance practices, including the use of real-world data, patient registries, and remote monitoring technologies. These approaches have helped to identify potential safety concerns and informed decision-making about the use of drugs.

Therefore, the COVID-19 pandemic has underscored the critical role of pharmacovigilance in ensuring the safety of drugs and the importance of continued efforts to improve, adapt pharmacovigilance practices in the face of changing circumstances.

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