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Impact of COVID 19 on Various Sectors of Pharmacy

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ABSTRACT

SARS-Cov 2 or the novel coronavirus has been posing a challenge in people's life since December 2019. Since then it has affected everyone's life in one way or the. It has the potential of getting transmitted through respiratory droplet spread or droplet nuclei that have settled on surfaces or via close contact. With COVID 19 affecting more and more people day by day, the health care system has gone beyond conventional practices to stop the further spread of the disease, the Pharmacy sector being one of the important contributors to this. Pharmacy services have improved access to medicines while ensuring the preventive measures suggested by the World Health Organization. From changes in the way of getting the medication history from the covid affected patients to medication acquisition, performing clinical trial activities, reporting adverse effects, and giving the discharge medication reconciliation wearing personal protective equipment and with limited patient contact, the workflow transition of pharmacists are commendable. They are also one of the first health care professionals to receive the COVID 19 vaccines. Continuity of the care by effective communication and follow-up will ensure a reduction in the complications of covid 19, the battle in which the pharmacist has a great role to play.

INTRODUCTION:

The world came to a halt when the SARS COV-2 virus-infected lakhs of people across the globe. The COVID-19 (coronavirus disease was first identified in China in December 2019).WHO picked up a statement about the 'viral pneumonia' on 31st December 2019 from Wuhan, China (1). Since then the respiratory illness has become a worldwide pandemic, infecting about 107,137,839 people and almost 2,340,535 has lost their lives and affecting almost 183 countries.(2) COVID-19 affects different people in different ways. Most infected people will develop mild to moderate illness and recover without hospitalization. Most common symptoms: fever, dry cough, and tiredness. Two types of tests are available for the diagnosis of covid-19. Which are?

For detection of the virus;

- Reverse transcription-polymerase chain reaction
- Isothermal amplification assays
- Antigen tests look for antigen proteins from the viral surface.
- Imaging studies
- Serology tests test blood and can identify once-infected people who have recovered because of the presence of IgG and IgM antibodies.

To date, there are no specific vaccines or medicines for COVID-19. Treatments are under investigation and will be tested through clinical trials (3).

- Mild COVID-19 cases may be given symptomatic treatment such as antipyretic (Paracetamol) for fever and pain, adequate nutrition, and appropriate rehydration. Tab Hydroxychloroquine (HCQ) may be considered for any of those having high-risk features for severe disease (such as age> 60; Hypertension, diabetes, chronic lung/kidney/ liver disease, cerebrovascular disease, and obesity) under strict medical supervision.

- For moderately severe cases, isolation of the patients must be required. For such patients oxygenation to reach the target sPO2 may be required. Tab. Hydroxychloroquine (400mg) BD on 1st day followed by 200mg 1 BD for 4 days is given. IV Methylprednisolone

0.5mg/kg is given for 3 days in case if the inflammatory marker increases. Prophylactic anticoagulation with UFH or LMWH (preferably enoxaparin 40mg SC) is also given.

- For severe cases of covid-19; early supportive monitoring and beginning of the therapy with oxygenation must be given. Conservative fluid treatment and High – Flow Nasal Cannula oxygenation (HFNO) or non – invasive mechanical ventilation for alleviated respiratory distresses is provided.

Also,an investigational drug, **Remdesivir** (with emergency use authorization) has been introduced. Pharma major Cipla launched its generic version of Remdesivir at Rs 4,000 per vial in India.

It used when an individual has moderately severe infection under the following conditions:

(Those on oxygen) with none of the following contraindications:

- AST/ALT > 5 times Upper limit of normal (ULN)
- Severe renal impairment (i.e., eGFR< 30ml/min/m2 or need for haemodialysis)
- Pregnancy or lactating females
- Children (< 12 years of age)

Convalescent plasma (Off Label) may be considered in patients with moderate disease who are not improving (oxygen requirement is progressively increasing) despite the use of steroids. The dose is variable ranging from 4 to 13 ml/kg (usually 200 ml single dose given slowly over not less than 2 hours.

Tocilizumab (off-label) may also be considered in patients with moderate disease with increasing oxygen demand. The dose is 8mg/kg (maximum 800 mg at one time) given slowly in 100 ml NS over 1 hour; the dose can be repeated once after 12 to 24 hours if needed.

As the pandemic hits more and more people, pharmacists as frontline health workers have been there from the beginning. Pharmacists globally are providing services in the form of, TRIAGE services, meeting the patients, and reducing the patients' burden due to the disease and hospital practices. Pharmacists are also working to providing home deliveries, as well as dealing with the increasing number of patients coming through to pharmacies with other ailments.(4)

Although the community pharmacists have always been there from the beginning of the outbreak by giving direct access to the medications to the public, people working in various other sectors of pharmacy have been contributing in their way and coping with the changes occurring due to the pandemic.

CLINICAL PHARMACISTS

One of the fundamental duties of clinical pharmacists is to ensure the proper provision of medications to patients. Their role has been crucial during the outbreak because, in such emergencies, various limitations can occur such as a shortage in supply of drugs. The COVID-19 has resulted in the global shortage of various drugs (Ex: hydroxychloroquine). (5). so by suggesting an effective therapeutic alternative must be done by the clinical pharmacist. They can contribute by developing a team for monitoring the drug supply that responds effectively when a drug shortage occurs. Also prioritizing and allocating the available drugs to the most needed patients can be taken up by the clinical pharmacists (6).

Pharmacists as part of the health care team can assist by allotting time for the administration of drugs to the patients, thereby limiting the unnecessary entry into the room and hence preventing the spread of COVID-19(7). Educating the patients regarding the drugs and possible adverse reactions that can occur also helps in a major way.

Lastly, the pharmacist can provide support to the patients by interacting with them and ensuring their service during emergencies, especially the community pharmacists. They can be considered as a trusted source in times of public health emergency. Pharmacists must educate their patients and the public on effective strategies to prevent the acquisition and further spread of infection (e.g., optimal hand hygiene, social distancing, staying home if having respiratory symptoms), symptomatic relief, from the knowledge acquired from reliable sources.

CLINICAL TRIALS

The SARS-CoV-2 virus has also shaken up clinical trials across the world. From April to May 2020 a survey has been conducted to understand the perspective of investigators regarding Clinical trials during the COVID-19 pandemic in 61 sites in Russia (8). It was found that only about 78% of the researches was going on by adapting to the situation, the rest 22% was somehow affected by the lockdown. But this is not the case in every country especially in the case of enrolment. In march 2020 studies in china showed a decrease of

enrolment by about 68% compared to the enrolment in 2019.The pandemic also marked the decrease in studies in various therapeutic areas i.e. endocrine(80%), cardiovascular (70%), CNS(68%), oncology(48%)(9).

Various health care companies have shared the extent of Covid-19's impact on certain on-going trials. Not only in enrolment, but a trial has become more challenging because of the

- unavailability of the study participants for in-person visits due to the quarantine,
- the variation in lockdown periods across the geographies,
- Multispecialty hospitals that conduct the trials may increase the chances of the participant getting infected.

It is during times like these, that technology comes to use. Effective use of artificial intelligence and machine learning can help to an extent. With digitalization, data standardization, increased participation (due to less reluctance to travel to the study site), increased diversity in the participants enrolled and lower cost to conduct the study can be ensured (9).

Incorporation of technology into clinical trials may also have its difficulties. It will be the responsibility of the healthcare companies to ensure the data transparency and privacy of the participants which is of utmost importance.

As restrictions due to covid-19 continue to exist, another possible way to conduct trials is by home visits. It can help improve the way by which participants see the trial thereby easing the process. But complex study design, tight timelines, busy clinical operations teams, and overburdened sites can sometimes make home health feel like yet another moving piece to manage. There are tremendous possible ways through which variability can occur. Some are (10):

- Amount of protocol-specific training required.
- Level of engagement during a visit.
- On-site processing requirements.
- Drug or sample stability.

- Recruitment goals.

Home visits during a trial may not be ideal for studies. It may require imaging reports or in-person meetings with the physician might be inevitable in some studies. This can be tackled by making use of a high-quality medical team and telemedicine technology. For example, Home visit nurses can also perform intraperitoneal (IP) injections, including working with carefully temperature-controlled medications or those that have to be reconstituted right before application. Thereby, ensuring protocol compliance also.

PHARMACOVIGILANCE

There are several programs at the national and international level that work to reduce the risks to patients and to establish worldwide pharmacovigilance standards and systems. The key health authorities such as the US Food & Drug Administration (FDA), European Medicine Agency (EMA), and UK Ministry of Health and Regulatory Authorities (MHRA) have accepted the fact that safety reporting has become challenging due to the ongoing pandemic.

Various countries use diversified methods to report an adverse event. Although many countries have adopted newer methods such as E2B (considered as an international standard for reporting ADRs and for effective transmission of ICSR by ICH), emails, etc. many authorities and agencies still use traditional methods of data reporting such as hand reporting. And many agencies such as IRBs, Ethics committees, however, demand the safety reports to be submitted in handwritten forms or couriers. This kind of safety reporting has become more challenging during the COVID 19 pandemic (11).

Below is the specific response guidance put forward by ICH for various types of COVID 19 related reporting (12).

ICH E2BR3 and R2 – COVID-19 specific guidance for certain elements (complete guidelines for ICH E2B(R2) and E2B(R3) at ICH-ESTRI)

E2B(R3)	E2B(R2)	Description	Guidance for COVID-19 related reporting
C.1.3	A.1.4	Type of report	[1=Spontaneous report], [2=Report from Study]
C.5.2	A.2.3.1	Study name	If applicable *NB! This information is searchable in VigiLyze.*
C.5.3	A.2.3.2	Sponsor study number	If applicable
C.5.4	A.2.3.3	Study type	If applicable [1=Clinical trials], [2=Individual patient use (e.g. 'compassionate use' or 'named patient basis')], [3=Other studies (e.g. intensive monitoring)]
D.7	B.1.7	Relevant medical history and concurrent conditions	Use this section to capture e.g. co-existing risk factors and underlying conditions.
D.9.2.r.1b D.9.4.r.1b	B.1.9.2b B.1.9.4b	Cause(s) of death Autopsy-determined cause(s) of death	If applicable, this information is coded using appropriate MedDRA terms, reporter's original words as free text (Free text in D.9.2.r.2 and D.9.4.r.2 respectively for E2BR3).
E.i.2.1b	B.2.i.1	Reaction/event	The MedDRA LLT most closely corresponding to the reaction/event as reported by the primary source should be selected. *NB! Therapeutic response in off label use can also be coded here using MedDRA; terms that may apply are e.g. "off label use", "therapeutic product ineffective for unapproved indication" or "therapeutic product effective for unapproved indication"*
F.r	B.3	Results of Tests and Procedures	Use this section to structure tests and procedures relevant to the investigation of the patient, e.g. positive results to SARS-Cov-2 testing.
G.k.7.r.1	N/A	Indication as reported by primary source (free text)	Indication as described by initial reporter *NB! This information is not available in VigiLyze due to R3 to R2 conversion.*
G.k.7.r.2b	B.4.k.11b	Indication (coded)	Use appropriate term(s) available in current version of MedDRA[1] *NB! If multiple indications – provide most relevant indication first (e.g. COVID-19). This field is repeatable in E2BR3 but only first indication will be available in VigiLyze due to R3 to R2 conversion.*
G.k.10.r	N/A	Additional information on drug (coded)	For E2BR3 it is possible to code e.g. off label use in a structured way [11=Off label use] *NB! Available in Narrative section in VigiLyze due to R3 to R2 conversion.*
G.k.11	B.4.k.19	Additional information on drug (free text)	Capture any additional information about the given drug in free text, e.g. labelling information with regards to the reaction(s).

[1] *For countries that still use ICD terminology in ICSR reporting; WHO has issued Emergency use ICD codes for COVID-19 disease (https://www.who.int/classifications/icd/COVID-19-coding-icd10.pdf?ua=1) that can similarly be used to code indication.*

However, as several drugs are under trial, timely review of the incoming data and safety reporting has become more important than ever. With the resurfacing of several drugs such as Hydroxychloroquine, Lopinavir/Ritonavir, and with the use of new drugs such as Remdesivir, several adverse events are anticipated. Moreover, multiple vaccines of different types are under development, and the first participants in clinical trials have received injections. (A vaccine is under development in Oxford University and now undergoing phase III trial). Given the vast */scale of vaccines to likely result, monitoring of the adverse events is vital. Various authorities such as WHO-UMC have come up with ways to minimize delays in safety reporting so that countries can benefit from each other's experience as soon as possible. Transparency and honesty in reporting are unavoidable during this time. All of us need to be vigilant about detecting false information and patient in providing explanations and corrections that can help prevent harm.

WHO-UMC has come up with an update in their MedDRA version (MedDRA is short for medical dictionary for regulatory activities which consists of all the clinically validated terminologies). The MedDRA 23.0 which came to effect on 19th April 2020 included all the COVID 19 related terms to encourage the global incoming of data related to events specifically associated with the treatment of COVID 19. (13).

UMC has suggested the use of codes to retrieve the data related to COVID 19.By coding the indication of the suspected drug used for the treatment, with the terms available in

MedDRA, analysis of the safety reports can be made easier. In addition to demographic details, such as the sex and age of a patient, other details that are particularly useful for analyzing and identifying COVID-19 related cases for analysis are:

- relevant medical history (including concurrent conditions)
- the outcome of the reaction
- results of tests and procedures
- cause of death (if applicable)
- narrative, sender's diagnosis, and sender's comments

If the drug is given as a part of the treatment as an unapproved indication, everything including the response can be captured by MedDRA. Terms that may apply include

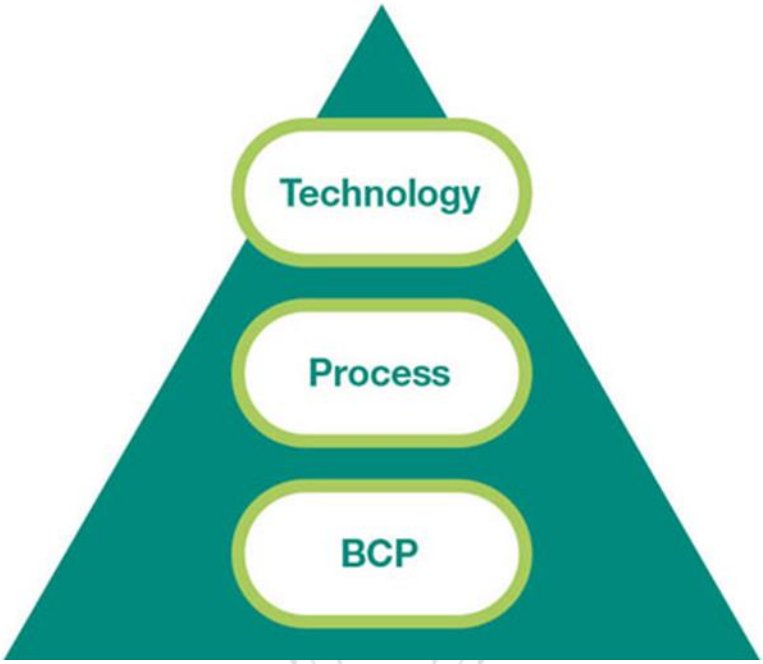
- off label use
- therapeutic product ineffective for an unapproved indication
- Therapeutic product is effective for an unapproved indication.

These terms can be used together with applicable **adverse reaction terms** to describe the individual case. Off-label use can also be captured as **additional information** on the drug. (14)

Also, new drugs, such as remdesivir, are being tried and several old drugs, such as hydroxychloroquine and lopinavir/ritonavir, are being repurposed. And reports suggest that various signals have been detected through the vigibase (15). And a large number of vaccines are under trials and various participants have received injections. So the monitoring and detailed reporting have become more important than ever.

At this time, perhaps more than ever before, pharmacovigilance experts have a vital role in demonstrating how our expertise, knowledge, and methodologies can help protect the safety of patients worldwide.

For achieving compliance in the safety reporting during the pandemic, a robust and responsive working plan is required. Making use of a strong business continuity plan (BCP), efficient electronic reporting system, the establishment of good communication with the sponsors and CROs will become vital.



SUMMARY:

Although Covid 19 has been affecting millions of people across the globe and is combined with fear and hope, some countries have come forward with vaccines claiming to have a potentially beneficial role in preventing coved 19. These vaccines may have a direct role in preventing the disease by activating the immune response or an indirect role by decreasing the viral load on individual patients.

CDSCO has given emergency use approval to Covaxin (made by the pharma company Bharat Biotech) and Covishield (made by Oxford-Astarzeneca, developed in the UK). When it comes to coaxing, both the manufacturer and drug regulator say it has the safety required and will provide a robust immune response, although it has been given approval many other drug networks and regulatory bodies are still skeptical with regards to the acceptance given for an 'incompletely studied vaccine'. And covishield, which contains a weakened version of the common cold virus (adenovirus), has proven to have 90% efficacy during its clinical trials.

Since vaccines are on their rounds, safety reporting has never been more important. Due to a large number of vaccinated people, safety monitoring has to be done to ensure the safety of

the vaccines. Intensive analysis and additional reports have to be taken from the vaccinated people to optimize the safe and effective use and there has been a series of adverse events since the vaccination like pain, malaise, weakness, rashes, nausea, and vomiting and if a new side effect is seen post-approval, it has to add in the package leaflet.

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