

A narrative review of the challenges, ethical frameworks, and guidelines in the setting of COVID-19 healthcare and research

Naheeda Hamza, Uma Kulkarni¹

Former MSc Research Ethics Scholar, ¹Professor and Additional Faculty, Centre for Ethics, Yenepoya (Deemed to be University), Mangalore, Karnataka, India

Abstract

The coronavirus disease (COVID)-19 pandemic has ever since its outbreak been perplexing healthcare generally at all levels. There is a need to identify, analyze and address the bioethical dilemmas that have emerged during the pandemic. This paper presents a narrative review of the published literature on the ethical issues, frameworks, and guidelines in COVID-19-related healthcare and research. An electronic search was conducted on PubMed, Google Scholar, and Science Direct using the search terms “COVID- 19”[AND] ethical issues, clinical trials, resource allocation, ethical guidelines, vaccine allocation. Articles between 2019 and 2020 focusing on ethics were included and analyzed. Fifteen full-text articles in English, one workshop summary, and 5 guidelines were identified and are discussed under the following themes: global response to the pandemic, allocation of resources, conduct of clinical trials, and fair distribution of vaccines and individual patient care. Despite the global and collaborative response to guide the healthcare sector throughout the pandemic, there have been some worrying repercussions in the form of increased vulnerabilities, precarious imbalances in resources, priority settings, exclusion of individuals or groups, exhaustions of healthcare professionals, impaired individual patient care, slowing down of non-covid research as well as scientific, ethical and logistic challenges in COVID and non-COVID research. These can be ethically justifiable only considering the seriousness and urgency of the pandemic. This paper presents some tenacious challenges that must be addressed if ethical reflection is to be effectively implemented in response to this pandemic.

Keywords: Coronavirus disease-19, ethical challenges, guidelines, healthcare, research, resource allocation

Address for correspondence: Dr. Uma Kulkarni, Centre for Ethics, Yenepoya (Deemed to be University), Mangalore, Karnataka, India.

E-mail: umakulkarni@yenepoya.edu.in

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INTRODUCTION

The coronavirus disease (COVID)-19 pandemic has been likened to a black swan event^[1] and the World War II economic scene due to the imbalances evidenced in the global healthcare system.^[2] Ever since the pandemic was

declared in March 2020, it has led to an extraordinarily high incidence of intensive care unit (ICU) admissions and mortality rates across the world. In this extraordinary context, adequate healthcare provision is challenged by inadequate resources.^[2] Several ethical concerns have

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arisen surrounding the management of scarce resources and end-of-life decisions. Simultaneously, all economies around the world have responded by taking measures to “flatten the curve;” border shutdowns, travel restrictions, quarantines, social distancing, and more.^[3,4]

Whereas bioethics is fundamental to healthcare, emergencies like pandemics have often challenged the ethical endeavor of the traditional guiding sources of medical ethics (the Hippocratic corpus or the “Four Bioethical Principles”).^[5] The World Health Organization (WHO) Global Health Ethics Team (GHET) in partnership with the African Coalition for Epidemic Research, Response, and Training, with representatives of National Ethics Committees (NECs) organized a 2-day workshop to prescribe practical measures and actions with respect to ethics review in pandemics and stated that to respond to contagious disease outbreaks and other health emergencies, nations do not rely only on adequate capacities for surveillance and infectious controls, nevertheless, adequate research capacities are warranted.^[6] It is evident in this crisis period that ethical dilemmas are inevitable and the challenges posed by the pandemic at various levels blur the guidance provided by the ethical principles.^[3,6,7] The paper seeks to explore the ethical challenges that the COVID-19 pandemic has posed.

The objectives of this paper are to explore the ethical challenges during the COVID-19 pandemic and review the frameworks and ethical guidelines related to COVID-19 from different countries across the globe published in 2020.

METHODS

The authors conducted a narrative review of the published literature on the ethical issues, frameworks, and guidelines in COVID-19 related healthcare and research. Due to the novelty and practice-oriented nature of the topic under investigation, the scope of the literature search took account of various databases including Google Scholar, PubMed, Science Direct, and other search engines that included non-peer reviewed sources such as conference papers, international organization frameworks from sources such as the WHO and United Nations Educational, Scientific and Cultural Organization published between 2019 and 2020.

SEARCH STRATEGY

In March 2020, an electronic search was conducted on PubMed, Google Scholar, and Science Direct using the search terms “COVID- 19” (AND) ethical issues, clinical trials, ethical challenges, resource allocation, ethical guidelines, vaccine allocation. The search was also carried

out on Science Direct using the same keywords [Table 1]. Overall, 15 full-text articles in English, one workshop summary, and 5 guidelines were identified and considered for review [Table 2] after excluding duplicate articles and those that were not focused on ethical issues/challenges/guidelines in COVID-19.

RESULTS

The article describes the ethical issues under the following themes: Global response to the pandemic, allocation of resources, conduct of clinical trials and fair distribution of vaccines, and individual patient care.

Global response to the pandemic

After declaration of the COVID-19 pandemic, countries across the globe instituted advisory bodies for building ethical frameworks and statutory branches to ensure compliance with ethical practices. Justifiably, the demand for these bodies to make provisions on ethical guidance has significantly grown in the urgent and rapidly changing context of the pandemic.^[8] In this view, the GHET seeks to support the NECs by setting up directions in response to the needs, facilitating communication systems, partnership, and sharing between NECs from around the world to help countries respond to the ethical challenges posed by COVID-19.^[9,10] Furthermore, the GHET in collaboration with the Global Network of WHO working with Centres for Bioethics has established a network of institutions in different locations worldwide. Experts in these centers strive to enrich their ethical support to WHO’s effort to provide guidance to its Member States.^[10] The GHET works to strengthen communication, collaboration, and cooperation in these endeavors. Congruently, the Public Health Emergency Preparedness and Response Ethics Network alongside the WHO and some key associates like Fogarty International Center, Global Forum on Bioethics in Research, Global Health Network, Global Network of WHO Collaborating Centres; built pre-existing expertise and resources to provide real-time, trusted, contextual support to communities, policymakers, researchers, and responders concerning the ethical issues arising out of global health emergencies.^[3]

Need for ethical guidance locally

Although guidance can be offered globally on ethical decision-making at hospital and public health policy level, there are challenges in their implementations locally. The health organizations and systems across countries are diverse, and the cultural and socioeconomic context is unique, thereby creating a need for ethical guidance locally.^[7,11] The priorities vary from country to country

Table 1: Search strategy adopted for review of articles between 2019 and 2020

Date	Database	K1	K2	Results
February 28, 2020	PubMed	COVID-19 pandemic	Ethical issues	2,322
March 28, 2020	Google Scholar	COVID-19 pandemic	Clinical trials	1,84,000
April 05, 2020	PubMed	COVID-19 pandemic	Ethical challenges	420
May 25, 2020	PubMed	COVID-19 pandemic	Resource allocation	688
June 10, 2020	Google Scholar	COVID-19 pandemic	Ethical guidelines	362
August 25, 2020	PubMed	COVID-19 pandemic	Vaccine allocation	148
October 20, 2021	PubMed	COVID-19 pandemic	Stigma	674
October 20, 2021	PubMed	COVID-19 pandemic	Communication barriers	414
October 20, 2021	PubMed	COVID-19 pandemic	Isolation	18,971
October 20, 2021	PubMed	COVID-19 pandemic	Social media	3950

COVID-19=Coronavirus 2019

Table 2: Fair allocation of vaccines based on priorities (Source: World Health Organization 2020)

Priority population	Rationale for prioritization
Those at greatest risk of becoming infected and seriously ill	Maximize benefit of vaccine
Those who are vaccinated would prevent the spread of the virus to a great extent	Maximize benefit of vaccine
Those who have volunteered to participate in research aimed at developing the vaccine	Reciprocal obligation to those who were voluntarily put at risk to aid in this effort

and includes allocation of resources, priority-setting, public health surveillance, physical distancing, healthcare worker's rights, and obligations to conduct clinical trials among others.

Social impact of lockdown measures

The COVID-19 pandemic has impacted all segments of the society, with the declaration of lockdown measures. Certain individuals or groups have been most vulnerable, such as those at extremes of ages, indigenous groups, those with limited financial abilities, or persons with disabilities.^[12]

Socio-economic vulnerability

Early evidence revealed that socio-economically poor groups encountered the worst consequences of lockdown for various reasons- employment was lost, crowding disallowed physical distancing, poor sanitation issues and lack of safe running water affected personal care, the homeless were unsheltered and unprotected and finally, healthcare facilities were unaffordable. These consequences were far more maleficent among refugees, migrants, or displaced persons.^[13] Policies are imperative to ameliorate the social crisis thus created to address issues of inequality, exclusion, discrimination, and unemployment in the medium and long term.^[3] A comprehensive, universal social protection system is the need of the hour to protect workers, safeguard them from poverty, and empower them to manage and overcome the crisis through the provision of basic income security during and beyond emergency situations.^[4] According to Lewnard and Lo,^[7] quarantine and physical distancing measures recommended to restrict the rapid spread of infection and thereby mortality, have led to job losses of about 11.6 million people amounting to more

unemployment in 2020 when compared to 2019. Loss of jobs and income have significantly affected those already living in poverty, or those working unprotected for layoffs and pay cuts, and those in precarious employment.

Elderly individuals

While social distancing is essential, its inapt implementation can deepen social isolation of the elderly, who are faced with greater health risk and unable to support themselves when they may need most.^[6,7,13]

Persons with disabilities

Limited access to healthcare services and support systems and the presence of pre-existing health conditions can add layers of vulnerability to persons with disabilities. Some forms of disabilities may deprive them from health information and health provisions, further limiting accessibility and timely healthcare. The impact is disproportionately more likely in institutional settings.^[4]

Impact of mandatory testing and public disclosure of infectious status

Even though testing for COVID-19 is made mandatory for the greater public good, the decision widely questions the respect for individuals owing to the stigma they face in the society due to stereotyping. Isolation, quarantine and disclosure of positive results gave rise to stigma not only of the affected individuals and family members, in society and workplaces but also of the treating healthcare workers.^[14] Unfortunately, the occurrence of stigma exists beyond what science can explain about COVID-19 and is perpetuated by the fear of the unknown and misinformation.^[15] A survey during the lockdown showed that about 61%^[16] of the Indian population are affected with mental health

problems owing to lockdown measures. Mental health problems have stemmed from mandatory testing for COVID-19, stigma attached to positive results and other challenges such as prolonged periods of isolation, social distancing, lockdowns, economic slowdown, closure of schools, workplaces, sporting activities and venues of entertainment (pause in normal life).^[17]

Impact of public dissemination of health information related to the pandemic

During the COVID-19 pandemic, social media, which is the fundamental source of information to the layperson, has had a great impact in causing panic and fear among the lay persons in the society.^[18] This resulted in undue publicity given to some early treatment, instances of hoarding and shortages of medicines, panic admissions to hospitals straining already scarce healthcare resources, and unnecessary investigations such as magnetic resonance images or computed tomography scans. Social media platforms have also been implicated in the surge of vaccine hesitancy.^[19] There have been reports of stocking of specific products like masks, soaps, sanitizers and disinfectants leading to hoarding and panic shopping.^[20] The uncontrolled dissemination of misinformation on social media has led to an “infodemic” with propagation of false information about the disease, its origin/transmission, treatment leading to stress, anxiety and harm.^[21] Therefore, there is a need to regulate social media postings about health information and responsible usage of such platforms.

Need for optimization of healthcare resources

The COVID-19 pandemic presented an unprecedented demand on the available healthcare resources owing to the high incidence of hospital and in particular, the ICU admissions, worldwide. Governments, international agencies, and health systems are obliged to ensure, to the best of their ability, adequate provision of healthcare for everyone (healthcare for all) practice.^[6] Optimization of limited resources, therefore, requires that the concerned authorities make extreme choices, some of which may be ethically justified whereas the others may raise ethical concerns for all the stakeholders: patients, medical personnel, general public, and policymakers.

Existing guidelines

Many ethical outlines have been drawn to help resolve the ethical challenges of coping with limited resources and human staff, and guide allocation of resources in an ethical and fair manner.^[11] However, their application depends on the type of healthcare resource, the context, and the stage of the pandemic. Furthermore, during the application of

ethical guidelines in the allocation of resources, the amount of resources that are available must be considered.^[2,22]

Infrastructure management

One of the most urgent needs of COVID-19 management was ICU infrastructure, even in resource-rich countries. Policies were in place where hospitals procured more ICU beds and facilities, upgraded the current ICUs, created step-down ICUs, procuring ventilators, coordinated the transfers of patients to hospitals with available ICU beds, acquiring vaccines and medicines, etc., in an attempt to mitigate the shortage.^[3,11]

Priority settings

The emergency and serious nature of the pandemic has forced tragic choices of setting priorities and rationing resources, which can be ethically justified only considering the high magnitude emergency setting. It would be considered ethically inappropriate to exclude certain population groups from being allocated a resource like ventilators, particularly when capacity is available. However, when resources are limited, allocation of resources ought to be guided by well-established, generally applicable ethical values, and any act of exclusion should be adequately justified.^[3]

Prioritisation based on medical risk factors

When resource development measures fell short, hospitals began to prioritize patients with better prognosis; and even fast-track withdrawal of life support in ICUs.^[11] Identifying high-risk characteristics of an infectious pandemic is difficult in the early stages since disease characteristics can only be identified after the infection has widely spread. In the COVID 19 pandemic, older individuals over 60 years of age were identified as a high-risk factor. This characteristic was significant and relevant to influence priority setting while allocating resources. Therefore, it was incongruous to use critical care triage guiding principles that have age cut-offs that deprioritize or exclude those aged over 60 years. As such, Jones^[23] states that the provision of care in a contingency setting inevitably requires decisions that assume the hierarchy of priorities to be reflected in the different interventions. Various care teams are charged with the responsibility of assessing the clinical needs of every patient, with; severity and urgency, and weighing the response according to the principle of equitable distribution of available resources. This is in response to the scarcity of resources which is a highly demanding responsibility.^[3]

Prioritization based on population characteristics

Immaterial attributes of the populations within countries, such as ethnicity, race, or creed, should not play a role in the

resource allocation during pandemics and all individuals or populations must be treated with equal respect and fairness. However, contextual circumstances may result in different decisions in every pandemic, although the ethical principles that apply to resource allocation might be the same.^[3]

Fair distribution of vaccines

The important ethical considerations that individual governments, manufacturers of vaccines, and sponsor need to consider during this COVID-19 pandemic is to guarantee an impartial distribution of vaccines at global level, that is, all countries are equally defenseless (vulnerable) to COVID-19 and have a communal responsibility, pivoted in solidarity, to collaborate with other countries to mitigate the outbreak and the spread.^[3,24] The government of each country has a special obligation to its citizens, nevertheless, a fair allocation of vaccines worldwide requires them not to simply appeal to self-interest, claims of resource ownership, and the prioritization of compatriots; but that vaccines should be allocated in a way that prioritizes those who fall into some categories and even more for those with direct needs as advocated by Thomas *et al.*^[25]

Summarily, a fair process for the allocation of limited resources during outbreaks must promote certain ethical values of transparency (the decisions and justifications should be made available to the general public); inclusiveness (those affected by allocation decisions – including individuals, communities, or countries – should be able to influence the decision-making process as well as the decision itself); consistency (such decisions should align with the ethical practices ensuring that all persons in a category are treated same) as stated by the WHO.^[3] Conversely, there is a need for evaluating the current system, because a fair system produces solidarity and trust among partners, which are essentials to the successful and sustained collective response indispensable for allocating effectively the resource and dealing with any outbreak.^[23,26]

Conduct of clinical trials

Two alarming characteristics of COVID-19 infection are rapid person-to-person transmission with an $R_0 = 5.7$ ^[27] and the mortality rate of 5.36–109.61 per 1,00,000 population globally.^[28] Therefore the biggest challenge posed by COVID-19 to the medical fraternity is to identify drugs which will reduce severity, hospitalization, and mortality caused by COVID-19 and vaccines which will reduce the infection rate. The COVID infection is yet to be understood. Therefore researchers have to be very careful in selecting the study design and the investigational product for a clinical trial.^[29] Clinical trials on a global scale require recruitment of participants which can be greatly impacted

by stringent measures taken by countries worldwide to reduce transmission of infection such as lockdown and travel restrictions. The Phase 1 clinical trial requires thorough monitoring of the patients with numerous in-patients and outpatients unit visits which can pose an additional risk factor for SARS-CoV-2 infection.^[30] Driven by the inadequate access to healthcare amenities, restricted travel options, self-isolation throughout in many countries resulted in difficulties in conducting and implementation of clinical trials with ethical bounds or acceptable standards. Consistent with this, Care *et al.*^[8] mentioned that mitigation efforts against COVID-19 interfere with all aspects of a successful clinical trial: efficient randomization, intervention adherence, delivery, and outcome collection.

Non-COVID studies

In addition, quarantine, isolation, and social distancing limit access to adequate health care institutions alongside shortages of medical resources and staff, leading to suspension or termination of most non-COVID-19 trials.^[6] Such that large pharmaceutical manufacturers such as Eli Lilly, Merck, Pfizer, and Bristol-Myers Squibb have all witnessed and declared that there are delays in their enrollment for ongoing studies and initiation of future studies. Biopharma Dive^[31] on May 15, 2020, announced that almost 100 companies and 240 trials have experienced disruptions; and the COVID-19 pandemic threatens to set back non-COVID-19 clinical trial research by several years. Apart from participant recruitment, planning and executing of clinical trials pose challenges, the crisis has had a major impact on clinical trials already ongoing as well as trials planned for the near future; where European Union Commission together with the European Medicines Agency and other stakeholders responded by issuing guidelines for sponsors, sites, and researchers on the administration of clinical trials in the course of the coronavirus crisis.^[32] Issued in March 2020, the harmonized guidance on the “Management of clinical trials during the COVID-19 pandemic,” outlined some emergency actions to minimize the negative effects like protocol deviations, serious adverse events and changes in informed consent to guide involved parties during clinical trials. General information on risk assessment and ongoing safety reporting to relevant authorities are of utmost importance for conduct of a clinical trial.^[29] However, the participants recruited for trials may often be severely ill patients, making informed consent very challenging. Hence, the EC has to review the protocol before the occurrence of emergencies.

Individual patient care

For individual patient care, it is imperative to have a healthcare professional who can provide such care

confidently, skillfully, and ethically. With the scarcity of human resources, special attention is warranted on the physical and mental exhaustion of professionals, promotion of conditions, and support to alleviate exhaustion and improve the clinical response capacity.^[33] Also, compassion fatigue and exhaustion syndrome often result from ethical conflicts related to the practice of intensive care, as with decisions to the allocation of available assisted ventilation equipment or the turning off of such equipment. At the same time, for the well being of the individual patient, family support is vital. However, hospitals have restricted the number of visits of family members to bare minimum to guard them from contracting the infection. In addition, hospitals have forbidden direct patient-family interaction and have resorted to newer communication modes. Patient care was also affected owing to policies pertaining to isolation and quarantine which were imposed to prevent spread of infection. On January 12, 2020, the WHO provided recommendations on the eligibility criteria for releasing patients from isolation and quarantine. Patients were discharged from isolation only if they had completely recovered and with two negative reverse transcription polymerase chain reaction results.^[34] These measures led to communication barriers which in turn led to fear, anxiety and a sense of insecurity among patients, family members, and the healthcare providers. The PPEs posed an added barrier for healthcare provider-patient communication, even making them unidentifiable. Families found it challenging to provide decisional and emotional support for the management of comorbidities.^[35] Therefore, the strict isolation and quarantine measures impacted patient care to a great extent.

Impact on non-COVID care

The diversion and reservation of healthcare resources including manpower and infrastructure to prioritize COVID-19 care posed a major hurdle to non-COVID-19 care. Many patients with chronic illnesses such as cancers, diabetes, and cardiovascular diseases suffered a major setback due to this. Rehabilitation facilities have been disrupted in 63% of countries across the globe. COVID-19 significantly impacts health services for non-communicable diseases.^[36] While this was to some extent inevitable, there should be some systems set up to take care of this during future pandemics, especially prolonged ones.

CONCLUSION

The COVID-19 pandemic has posed several ethical challenges to humankind. There has been a global response with international collaborations to guide the healthcare sector in handling this infectious emergency in

a befitting manner. However, some bitter repercussions are evidenced which can be ethically justifiable only considering the seriousness and urgency of the pandemic. The lockdown and other restrictions have led to an increased vulnerability of the already vulnerable groups and have led to stigmatization of individuals and families. In healthcare, it has led to precarious imbalance in resources, resulting in strategies like priority setting and exclusion of certain groups of people or populations. The pandemic has impacted healthcare of individual patients as badly as it has impacted the healthcare professionals through exhaustion and stigma. The pandemic has reflected on the non-COVID healthcare and research and at the same time posing scientific, ethical, and logistic challenges.

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