

Nearly three years have passed since the novel coronavirus pandemic was declared a Public Health Emergency of International Concern (PHEIC) by the World Health Organization.

This volume brings together several distinguished scholars to analyze what has been done in selected countries (India, Italy and the United States) - and what needs to be done, more broadly, going forward - for tracking and tackling the lingering health and socio-economic impact of the pandemic.

The present volume is a reminder of the need for continued focus on tracking and tackling Covid-19.

The pandemic is still not over.

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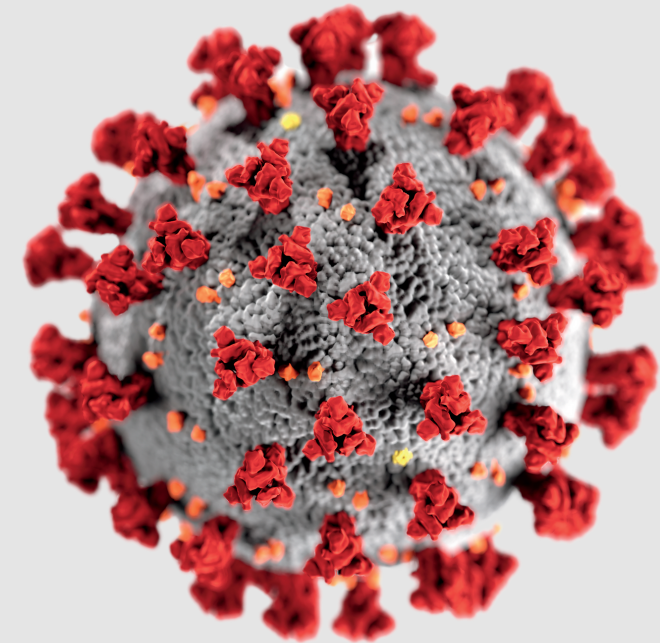
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TRACKING AND TACKLING COVID-19

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Towards Ethical Biomedical and Health Research During the Covid-19 Pandemic

The Case of India

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Abstract

The unprecedented challenges imposed by Covid-19 required urgent research initiatives. A large number of research studies were led by institutions spread across the country (India) to find answers to the novel challenges imposed in clinical medicine, epidemiological investigations, basic science questions, socio-behavioural studies, implementation research and also in translation of research findings for finding better public health interventions and policies in a time-bound manner. A certain level of ethics preparedness was already present as during the past decade, the Indian Council of Medical Research (ICMR) had been working on a number of initiatives towards building ethics framework and research capacity to tackle disease outbreaks. This helped it to respond quickly and ensure that the research was conducted in a manner that ensured robust scientific and ethical standards. The country can boast of its strong ethical and regulatory framework in the form of national guidelines, policies and laws that

guide the conduct of biomedical and health research as well as clinical trials. The challenging times saw a lot of newer initiatives and steps being undertaken with the overall aim of ensuring safety and well-being of the public at large. This paper discusses some of the initiatives and steps taken during the challenging times with the hope that these experiences will help us identify potential lessons and be better prepared for the future.

Introduction

The onset of the Covid-19 pandemic in India in January 2020 presented unprecedented challenges, and the country had to make a number of urgent decisions in order to ensure that clinical services as well as research do not suffer so as to protect the public at large. The Indian Council of Medical Research (ICMR) under the Department of Health Research (DHR), Ministry of Health and Family Welfare (MoHFW), Government of India is the apex institution promoting and formulating biomedical research, and was at the forefront of crisis response through well-designed and phased-out research initiatives and programs.¹ These were aimed at generating evidence to tackle the emerging situation through use of robust scientific research tools and methods. The ICMR Bioethics Unit also responded promptly to facilitate the ethical conduct of biomedical and health research across the country.²

The whole world was caught unaware and unprepared to tackle the rapidly spreading pandemic. Developing countries like India, with their large and diverse populations, had their own unique set of overwhelming challenges presented by the pandemic, impacting the economy, society, health (including prevalent diseases and national health programs), etc., necessitating attention to be directed to those who were underserved or marginalised to protect them from long-lasting adverse outcomes (Gopalan and Misra, 2020). A rapid public health response was critical step towards setting up systems to identify public health priorities, setting up goals and agendas, identifying ways of measurement for setting up our national policies and programs for surveillance, involving timely and systematic collection, analysis and dissemination

¹ <https://www.icmr.gov.in/> (accessed on 26 October 2022).

² <https://ethics.ncdirindia.org/> (accessed on 26 October 2022).

of data. Strong initiatives lead us to suitable public health actions, which involve not only funding and investments in infrastructure and human resources, but also actions, such as evidence-generation, building channels of right communications, sharing of data, filling knowledge gaps, apt use of available resources, setting up networks for collaboration, etc. Since the onset of the pandemic, ICMR had stepped in to take up a phenomenal leadership role in undertaking and supporting large research studies for identifying better ways of tackling the pandemic. It instituted a multi-prolonged approach to understand the disease and tackle it through its work with multiple stakeholders (GRID Covid-19 Study Group, 2020).

Recent initiatives

Over the last several years, ICMR had been working towards enhancing national capacity for early diagnosis of infections with an epidemic potential, and with the support of DHR, had set up a national network of well-equipped virus research and diagnostic labs with trained manpower for response during epidemics. The program was being coordinated at the ICMR-National Institute of Virology (NIV) in Pune. In the recent past, the labs were involved in testing for Zika, Nipah and other viruses. With the advent of Covid-19, the ICMR led major research initiatives in a time-bound manner to respond to the emergent situation and the needs of the country, whether it was in building capacity, expanding a large network of both public and private virus diagnostic laboratories, developing and validating test kits, developing the diagnostic capabilities of labs across India, quality assurance, undertaking several national sero-survey studies, supporting various genome sequencing consortium studies, undertaking research on environmental associations, animal-to-human transmission, studies on socio-economic aspects, mental health, socio-economic well-being and many other such research initiatives. In view of the numerous initiatives that the country took, the Covid-19 response in India was rapid, strategic and multi-pronged, adapting to the requirements of the evolving pandemic situation (Madhakar et al, 2021).

A large number of other new initiatives were also taken, such as the initiative towards setting up of a national clinical registry of

Covid-19³ and a national registry of pregnant women with Covid-19⁴ in India to collect good quality, real-time data on various clinical, epidemiological and outcome aspects of the disease. In addition, it also worked towards the creation of a number of guideline and policy documents, such as those related to treatment and management of Covid-19, safety protocols, clinical guidance for management of adult patients, appropriate recording of Covid-19 related deaths,⁵ framework for telemedicine guidelines for non-communicable diseases (NCDs),⁶ etc. Another milestone was the setting up of a national institute on One Health in Nagpur, which would cater to the need of undertaking systematic studies for outbreak investigations and tackling biosafety and biosecurity aspects, while enhancing the diagnostic capabilities of the country for various initiatives in the future (Chaudhari et al, 2021). All these initiatives required multiple efforts in engaging with various stakeholders, such as public policy experts, and collaborating with government as well as non-governmental agencies, private players and volunteers on various aspects of the battle against Covid-19. Efforts have been made to hold multiple engagement programs, including symposiums, call for proposals to collaborate, expand networks and have better participation and support for these initiatives.

There was a clear need to undertake research on a priority basis, but without making any compromises vis-à-vis scientific validity and ethical requirements. Close attention was needed on perceptions of ethical questions, altered or increased vulnerabilities, protection of research participants, especially those who were more vulnerable, researcher and participant relationships, issues related to ensuring scientific integrity of research, robustness of ethical review processes, transparency and accountability in research and other such matters. A certain level of ethics preparedness was already available in the country due to several ICMR initiatives undertaken for capacity-building in the recent past, such as availability of a strong network of centres across the country with appropriate manpower and resources, a well laid out ethical framework to promote good science and ethics, procedures for ethics review,

³ <https://bit.ly/3D9tlAP> (accessed on 26 October 2022).

⁴ <https://pregcovid.com/> (accessed on 26 October 2022).

⁵ <https://bit.ly/3NbbH43> (accessed on 26 October 2022).

⁶ <https://bit.ly/3zkuBzN> (accessed on 26 October 2022).

community considerations and measures to make science more holistic, sensitive and people-centric, focusing on local, social and cultural values (Mathur, 2020).

The socio-cultural ethos in India and its varying standards of health-care pose unique challenges. During these challenging times, the ICMR Bioethics Unit, which is also recognised as a WHO Collaborating Centre for Strengthening Ethics in Biomedical and Health Research, played a very important role in supporting the framework to guide and support ethical aspects of research being conducted in the country during the emergency situation.

National framework for research ethics

India has a strong framework for ensuring the ethical conduct of biomedical and health research as well as clinical trials in the country. Various efforts have been made to keep it updated, and there are national guidelines, policies as well as regulations in place that govern different aspects of the conduct of research, the process of ethics review and ensuring the quality of research. The framework duly safeguards the rights, welfare, well-being and safety of research participants. The related details that guide the implementation, monitoring, quality and ethical conduct of biomedical and health research or of clinical trials for approval of therapeutics in the case of epidemics/outbreaks are as follows.

1. The *National Ethical Guidelines for Biomedical and Health Research involving Human Participants, 2017* need to be followed for all types of biomedical and health research undertaken in India.⁷ The guidelines consist of 12 sections which discuss ethical issues pertaining to various types of research, such as clinical trials, public health research, socio-behavioural research and genetics research. They also discuss issues related to informed consent, research involving vulnerable persons, collaborations, research involving use of biological material or datasets, etc. The guidelines make it mandatory for research to be reviewed and approved by a duly constituted ethics committee before it is initiated. There are sections discussing

⁷ <https://bit.ly/3TBnpHv> (accessed on 26 October 2022).

ethical principles, general ethical issues as well as the responsible conduct of research focussing on the need to maintain research integrity. The guidelines for public health research clarify the differences between a surveillance study versus a research or a public health program because the distinction between them is often blurred. The guidelines carry a separate section on research during humanitarian emergencies and disaster conditions, and identify the need for pre-emptive preparation, and suggest a framework for prior planning for dealing with emergencies and outbreaks. This section discusses how an ethics committee can undertake an expedited review or hold unscheduled meetings to undertake ethical review in a time-bound manner. The guidelines already had a brief discussion on epidemics and humanitarian emergencies and research in such situations. But when the Covid-19 pandemic actually struck, it was realized that much more detailed guidelines are required.

2. *National Guidelines for Ethics Committees reviewing Biomedical & Health research during Covid-19 pandemic*: The ICMR Bioethics Unit responded very early, with these guidelines being prepared and released as early as April 2020.⁸ With this, India became the first country to come up with such a guidelines document to facilitate research across the country. The guidelines proposed ways to undertake timely and robust ethics review for systematic collection, analysis and dissemination of data for suitable public health action, information about the virus, its human interaction, diseases and their outcomes, determinants of infection and host response, and how to set up a robust ethical framework to support Covid-19 related research during the challenging pandemic time. It discussed the need not only for the review of Covid-19 research, but also highlighted the importance of the continuation of ongoing research studies with relevant changes as needed due to the new social distancing norms. It also discussed the need for continuing research on non-Covid-19 disease conditions since other infections, NCDs, etc. should not lose focus. This document provided updated information on organizing online ethics committee meetings and suggested, for the first time, that an online quorum may be

⁸<https://bit.ly/3fdqIFX> (accessed on 26 October 2022).

considered by the ethics committee in the changed times. It also suggested the need to be open-minded to accept new innovative methodologies, adaptive study designs, possibilities of using electronic documentation methods for ensuring informed consent processes, facilitating expedited committees and fast-track time-bound ethical reviews so that research does not get delayed. It urged researchers as well as ethics committees to communicate better and respond to the requirements and the need of the hour so that research is robust, reviews are expeditious, but without making any compromise on the quality of research or the due protection of participants rights. The guidance suggested that ethics committees could appoint not only members, but alternate members, and invite subject experts or community representatives, according to the needs of the research protocol, to ensure robust, time-bound, competent and independent ethics reviews. It highlighted the need for ethics committees to guide researchers to try to develop methods to engage better with the communities, be wary of the 'infodemic', dispel unnecessary panic or fear by improving communication, use of advocacy methods, build extensive partnerships to collaborate and efforts to develop public trust. Conflict of interest management was suggested in the guidelines. Adapting to newer methodologies, technologies, adoptive designs, and being open to new ideas were suggested in the guidelines. Other important suggestions were to put monitoring mechanisms in place, encourage collaborations and look at increased vulnerabilities and safety of healthcare workers while reviewing research. Engaging with communities and looking at aspects of payments and compensations in case of research-related injury and benefit-sharing after research is over were other suggestions. The guidelines have also discussed the importance of taking care of psychosocial and mental health. They asked government agencies to have better research governance frameworks too for better coherence and concerted efforts leading to meaningful outcomes. They have suggested ways of adopting common ethics reviews for multi-centre research programs by a designated ethics committee, where local review can focus on site-specific concerns and local site monitoring. This would not only save time and efforts, but ensure better quality reviews and harmonization of research initiatives.

3. *Registration of ethics committees and research:* All ethics committees in India are required to register with central licensing authorities. Ethics committees that review clinical trials are required to register with the Central Drugs Standard Control Organization (CDSCO), and those that review biomedical research have to register with the DHR. The guidelines state that all Covid-19 related research should be registered with the Clinical Trial Registry of India (CTRI) to bring in better transparency, avoid duplication of research and promote collaboration. The CTRI is housed in ICMR-National Institute of Medical Statistics (NIMS), and collects information of clinical trials before any participant enrolment. The collected information includes details of participating study sites, investigators, sponsors, interventions and patient groups. The registration also requires uploading information regarding approval from the ethics committee and the CDSCO for clinical trials. Even though registration is mandated under the New Drugs and Clinical Trials Rules, 2019 (NDCTR, 2019), it was suggested as a good practice that all types of Covid-19 related research should also be registered voluntarily on the CTRI platform.⁹
4. *Regulatory framework for clinical trials:* The NDCTR, 2019 under the Drugs and Cosmetics Act, 1940, regulate new drugs, investigational new drugs for human use, clinical trials, bioequivalence studies, bioavailability studies and ethics committees in India. Under them, an ethics committee is required to register with the CDSCO – trials can only be conducted after its approval. In case of any serious adverse event during a clinical trial or a bioavailability/bioequivalence study, the ethics committee is required to analyse relevant documents pertaining to such event and forward its report to the central licensing authority. In addition, there are specific provisions for fast-track approvals during public health emergencies. The country has a strong regulatory framework in place for clinical trial registration and approvals.
5. *Capacity-building and quality assurance for ethics committees:* A very large number of capacity-building initiatives in the area of ethics have been implemented. ICMR had conducted one of the largest programs for the dissemination of national ethical guidelines

⁹ <https://bit.ly/3TEMQbj> (accessed on 26 October 2022).

between 2018 and 2019, reaching out to more than 8,000 stakeholders across the country. In addition, a large number of training workshops and courses had been organized to train ethics committees regarding their roles and responsibilities.¹⁰ Furthermore, for the purpose of quality assurance, an accreditation program has been put in place for ethics committees that review clinical research, coordinated by the National Accreditation Board for Hospitals and Healthcare Providers (NABH).¹¹ Under this program, there are certain laid down standards related to ethics committee accreditation process, which need to be adhered to for improving the safety of the process of clinical trials in India. It is an attempt at standardizing the quality of clinical research in the country. At present, the program is voluntary, and a large number of ethics committees are approaching NABH so that they are part of the quality assurance process.

Ethics committee tools

Over the last few years, a lot of efforts were made to develop comprehensive forms for ethics committees that would require researchers to submit relevant information about study protocols to ethics committees. This would facilitate the ethics review procedures, while the use of such standardized forms would also improve collaborative research programs. The ICMR common forms for ethics review proved to be a bonus during the pandemic for ethics committee functioning because these included checklists to ensure submission of only complete information by principal investigators, saving time on back-and-forth communications due to incomplete submissions. Further, this would help to harmonize reviews for multi-centric sites. Otherwise, every ethics committee has a different set of requirements for submission, which often delays research. These forms have formats for not only initial ethics review, but also continuing review, expedited review, exemption from review, CV formats, adverse event reporting formats, formats for genetic studies or epidemiological research, etc. These help

¹⁰ <https://bit.ly/3svO64F> (accessed on 26 October 2022).

¹¹ <https://bit.ly/3SD5or2> (accessed on 26 October 2022).

to ask relevant questions from researchers to facilitate timely ethics committee reviews.¹²

The ICMR Bioethics Unit also developed SOPs for ethics committees to fast-track ethics reviews as time was of essence and research needs of the times were enormous. This format laid down procedures for quicker turnaround of ethics reviews. It was made available to ethics committees across the country for conducting emergency reviews.

All these measures towards biomedical and health research as well as clinical trials were found to be very helpful during the Covid-19 pandemic in India.

Other ethical safeguards

Another important aspect was related to research involving human biological material and their datasets. There are complex issues related to informed consent process of datasets, samples collected for a clinical purpose and to be used for research. The ICMR national guidelines have a full section on using such datasets and bio-banking for future research, and there are various suggestions and provisions listed for taking waiver of consent under certain conditions. During Covid-19, one of the other very relevant concerns has been taking care of those who are vulnerable. Covid-19 has exposed people to additional risks related to discrimination or rendered them vulnerable due to isolation, quarantine or social distancing norms. Many people lost their jobs, many were rendered homeless and many had to migrate. Similarly, the elderly population became a captive population, with additional vulnerability in view of the higher risk of mortality due to chronic illnesses. The guidelines suggested ways of including them so that the benefits of research can also apply to them. However, any such research had to make sure that there are adequate measures to safeguard their rights and safety. The guidelines have provided more clarity on such topics and has been an important reference in these trying times. In a public health research study, on the one hand, there are rights of participants that have to be upheld and, on the other hand, are public health goals that have to be pursued.

¹² <https://bit.ly/3W2bZyj> (accessed on 26 October 2022).

A balance needs to be maintained between the two. The narrow boundaries between public health practice and research must be ethically dealt with, even as methods for data collection through surveillance, vital statistics, disease reporting, registry programs, preventive intervention, monitoring, program evaluation, disease notification, quarantine issues, etc. deserve close attention and planning to uphold the rights of individuals while catering to the need of the hour. Further, researchers should prevent an ‘infodemic’ – a new term coined by the WHO to ensure responsible reporting in the public domain.¹³

The ICMR guidelines also stress the need for ensuring safety and well-being of the healthcare workforce, making due provisions for their safety, their training on waste disposal and handling of infectious material, and also caring for their psychosocial well-being and mental health during the trying times. Another important aspect related to translation of research findings. It is important to plan, from the beginning, ways of sharing and giving back the benefits that emerge from research to the people or the communities who were part of the study, wherever possible. Provisions to take care of any study-related injuries, to medically manage the same, cover expenditures incurred by participants due to their participation in research, etc. must be planned in the budget so that participants do not incur any expenses. Further, the need for more transparency and accountability as well as publication of both positive and negative results has been suggested. The guidelines have discussed a large number of safeguards that researchers should plan, and it is important that the same are followed to impart better protections to the participants and the public at large.

The ICMR-Central Ethics Committee on Human Research has played a very important role in serving as a national ethics committee for reviewing large, multi-centric research studies conducted by ICMR and its network of institutions. This Committee also reviews complex ethics issues and guides ethics policy at ICMR. The Committee had to be reconstituted with members and alternate members to meet the demand of urgent, time-bound reviews. It has a multidisciplinary team of experts from a variety of fields who understood the need for, and passionately reviewed and guided, various ICMR-led research studies, whether it was biomedical research, clinical trials, epidemiological

¹³ <https://nyti.ms/3zcaPqf> (accessed on 26 October 2022).

research, basic sciences, sero-surveys, socio-behavioural research, program implementation research or other types of investigations. The multidisciplinary committee has met frequently with a shortened turnaround time for ethics review of research during this time, and guided ICMR to undertake high-quality research. It was involved in undertaking initial full committee reviews, expedited reviews, continuing reviews and monitoring of research undertaken by ICMR headquarters or other institutions.

The way forward

To conclude, it is time to further step up our pandemic preparedness, which ensures appropriate planning and set-ups to handle emergent situations in an integrated fashion, with the ultimate objective to bring it under the One Health platform. There have been enormous efforts at the global level, and India has been a part of them, and there has been a lot of collaboration that we have never seen before. The unprecedented times have encouraged us to move forward together to seek solutions and learn from innumerable examples of multiple collaborations that have happened on multiple platforms and levels. Further, there is a need for more and better engagement with all stakeholders who are part of the research enterprise, including the public. There are efforts to set up clinical trial networks, disease and data registration systems, surveillance programs, rapid action task forces on implementation, laboratory networks, better data recording systems and registries, and collaboration between agencies and partners to work together for a common cause. Various efforts and initiatives are required to establish the best, socially acceptable ethical safeguards in the best interests of the population. They will help ensure that public health measures and research undertaken is more responsive, ethical and acceptable to the public. This is also the time to come together for a common cause, to identify and share best practices to ensure a better and faster response by breaking boundaries and encouraging partnerships. All efforts must be made to safeguard the safety and rights of human beings in the research ecosystem. It is time to realise that for every research program, ethics has to be the central theme right from conceptualization to planning, implementation, monitoring and follow-up.

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