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Challenges faced by ethics committee members in India during COVID-19 pandemic: A mixed-methods exploration

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***Background & objectives*: The COVID-19 pandemic had a distinct impact on scientific research and Ethics Committees (ECs). We conducted a mixed-methods investigation to understand the issues faced and solutions identified by ECs during this pandemic in India.**

***Methods*: A quantitative online survey form (30 members) and qualitative in-depth interviews (10 members) from various ECs were conducted. Thematic content analysis for qualitative and proportion analysis for quantitative data was carried out.**

***Results*: During the online survey, an average difficulty score, which was measured using the Visual Analogue Scale, was 5.3 (SD 2.1). Pressure for expedited approvals was felt by EC members with a drastic increase in the number of submission of research projects. The scarcity of information on investigational products (IPs) and requisite consent process posed major hurdles. Ongoing non-COVID studies and post-graduate dissertations were badly hit due to the shift in attention towards COVID-related research. Non-familiarity with virtual technology and lack of face-to-face interactions were highlighted as demerits. However, a few of the EC members welcomed newer methods, being time-saving, convenient and reducing travel hassles. Site monitoring and severe adverse event-related analyses were also negatively impacted upon. Solutions included the alternate methods of consenting (virtual, abbreviated), a detailed explanation of the protocol and IPs and benefits versus risk assessment.**

***Interpretation & conclusions*: Despite various challenges posed by the COVID-19 pandemic, the ECs in India steered well through the hurdles. Moreover, adapting a hybrid mode, technical training and updating guidelines were perceived as urgent by EC members.**

Key words Challenges - COVID-19 - Ethics Committee - functioning - research - solutions

The COVID-19 pandemic and subsequent lockdown in India not only affected the society at large but also the researchers and particularly ethics committee (EC) members as the number of proposals related to COVID-19, submitted for evaluation, increased considerably[1]. These proposals needed

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expedited discussion considering the national and global emergency. Importantly, the document titled 'National Ethical Guidelines for Biomedical and Health Research Involving Human Participants', 2017, published by the Indian Council of Medical Research (ICMR)[2], in subsections 4 and 12 elaborated upon the issues related to expedited approval. Research during 'Humanitarian Emergencies and Disasters' has been considered in this document as a topic, which could necessitate expedited approval. ICMR also published the 'National Guidelines for Ethics Committees Reviewing Biomedical and Health Research during COVID-19 Pandemic' on May 6, 2020[3], as an aid to the functioning of all the ECs across the country[4].

In the wake of the COVID-19 pandemic, while on one hand research activities were negatively impacted upon, on the other an increasing number of proposals for research on COVID-19 were being submitted to the institutional ECs for consideration. However, during this trying time, ECs, like other institutions, were facing constraints due to the impact of COVID-19 on their members at an individual level as well as restrictions on physical meetings and discussions. Preparedness of the ECs appears to be an important component to deal with such public health emergencies[5].

In this study, we aimed to understand how difficult it was to conduct activities of ECs during lockdown and other off and on restrictive measures for principled conduct of biomedical research. We inquired how difficult it was for the ECs to function during this difficult time and also the steps taken to overcome the challenges. A mixed-methods research approach was followed to explore such issues in-depth and to generate a thorough understanding of the processes, which took place during COVID-19.

Material & Methods

The current study was conducted during February 2021 to April 2022 after clearance from the Institutional Ethical Committe (IEC) of ICMR-National AIDS Research Institute (NARI), Pune, India. The study was conducted in line with the principle of Declaration of Helsinki and an informed written consent was obtained from all the study participants. It was a mixed-methods investigation, comprising both quantitative components in the form of an online survey and qualitative inquiry through in-depth interviews (IDIs). A list of ECs registered with the Central Drugs Standard Control Organisation (CDSCO), Government of India, was prepared beforehand, and subsequently, another list of institutions conducting research during the COVID pandemic was drawn up from the Clinical Trials Registry of India website. The participants in this study were EC members of government and private medical colleges, research organizations and private hospitals with valid CDSCO registration numbers and who had participated in reviewing COVID-19-related research protocols during the pandemic. The telephone numbers of the Member Secretaries of the ECs was accessed by calling the respective institutional landline numbers and also through our database of contacts of various institutes where ICMR-NARI had established a collaboration. The EC Member Secretaries in turn helped us in contacting the members of the ECs through email and also telephonically. An online survey link was sent to 298 members of 48 ECs to which thirty EC members responded. The members were sent three consecutive reminders at fortnightly intervals. Major reasons for non-response were lack of time and unwillingness to participate.

Sampling: Sample size for the online survey was determined as 96 with an anticipated standard deviation of difficulty score (defined below) as 2 and absolute precision of 0.4[6]. An online survey link was sent to 298 members. Due to non-response, the target sample size could not be achieved and only 30 individuals out of 298 returned filled online forms.

The EC members participating in the survey were provided with the Visual Analogue Scale and were requested to mark a point on it to indicate overall perceived level of difficulty in the arrangement of EC activities during COVID time taking into account all the different components of EC functioning. The scale ranged from 1 to 10 with 1 as 'not at all difficult' and 10 as 'very difficult'. Henceforth, this will be referred to as a difficulty score. Given that the outbreak of COVID enforced sudden changes in the functioning of ECs, we presumed that the difficulty score was close to 1 (not at all difficult) during the non-COVID period.

Under the qualitative component of the study, a purposive sampling technique was followed to recruit participants for IDIs till the saturation in responses was achieved. We included interviewees with different roles in EC for in-depth interactions to obtain as wider viewpoints as possible in our exploration. No participant was enrolled in both quantitative survey and qualitative inquiry. Thus, a total of mutually exclusive 30 online forms could be filled, and 10 IDIs were conducted.

Study tool: Guides and probes were developed to conduct qualitative IDIs based on literature review and suggestions obtained from Scientific Advisory Committee and EC members. These were constructed taking into consideration certain domains, which were identified for exploration. These guides were pre-tested through mock interviews to check for their appropriateness, and accordingly, certain changes were made to achieve easy comprehension. The following domains were explored; 'problems faced', 'experiences with virtual meetings', 'expedited review and approval process, waiver of consent as per the National Guidelines for ECs Reviewing Biomedical and Health Research During COVID-19 Pandemic; waiver of consent under 4.3.1[3], 'solutions applied', 'perceived merits and demerits' and 'innovations if any'. A semi-structured questionnaire was developed covering the aforementioned domains for the online quantitative survey as well, which was pilot tested before the finalization (Annexures I). The questionnaire for the online survey was designed based on different literature available and having a discussion with the Institutional Scientific Advisory Committee and the IEC of ICMR-NARI. It had both close-ended and open-ended inquiry.

Data collection: The project interviewer was trained on qualitative research methodology through his earlier involvement in qualitative investigations. A checklist was used for every IDI to maintain consistency in quality. Eight IDIs were conducted through online mode. Each participant was contacted telephonically first by the investigators explaining the purpose of the study following which a consent form was sent via e-mail to the respective participant. Once scanned signed copies of the consent forms were received by the investigator, further dates and times for interviews were fixed as per the convenience of the participants. Two IDIs took place at the work premises of the participants as per their preferences. Privacy was maintained during these online IDIs. It was ensured that the members with different roles in ECs were included for in-depth interactions to reflect a comprehensive understanding of the chosen domains. All these members were from government and private institutions involved in reviewing COVID-19 studies.

The online Google Forms (Annexure I) was sent by email, and also through WhatsApp to the EC members. Of the 30 survey participants, 27 responded through Google Forms, while the rest three used paper-based questionnaires and sent them back to by email after filling in their responses.

Data analysis: Analyses for quantitative and qualitative components were carried out concurrently. All qualitative IDIs were conducted in the English language except one and were audio recorded. Subsequently, these were transcribed exactly verbatim, and the one IDI conducted in Marathi was transcribed first and then translated into English. Research investigators checked for the quality of transcripts to ensure that each viewpoint expressed by the participants was appropriately incorporated into analyses. Problems faced by the ECs during the COVID-19 situation and solutions devised by the committees were examined by undertaking content analysis. Inductive coding was done independently by the investigators. Any discrepancies in the codes were sorted out through mutual discussion and regular meetings. This helped in organizing codes into major or minor themes (categories). *In vivo* codes were applied to extract the perspectives or concerns of the study participants through their own articulation. Further analysis was carried out manually by both the investigators using hard copies of the translated transcripts.

An online quantitative survey automatically captured data in Microsoft Excel sheet. Data from three paper-based forms were entered manually. Quantitative survey data were analyzed using proportions and appropriate statistical tests. The difficulty scores were normally distributed (Shapiro–Wilk test P=0.994), hence t test for equal or unequal variances and one-way ANOVA were used to test the difference between means of the various groups, as appropriate for two or more groups.

Results

Participants' profile:

Online quantitative survey: The members responding through the online survey form were from different regions of India (2 from the Central zone, 7 from the East, 4 from the North, 2 from the South, and 14 from the West). The majority of the 30 online respondents were (20; 66%) males. The median age of the survey respondents was 51 yr (minimum-maximum: 34-77 yr). Survey respondents were from different backgrounds pertaining to the responsibilities discharged in their respective ECs such as chairpersons 4 (13%), member secretaries 6 (20%), basic medical scientists 4 (13%), social scientists 6 (20%), clinicians 6 (20%), legal

experts 2 (7%) and lay persons 2 (7%). Although 12 (40%) online survey participants were affiliated with more than one EC, their roles remained the same across these committees. The number of EC members affiliated with government institutions was 18 (60%) and private medical colleges and private hospitals 18 (60%) and three (10%) were affiliated with independent ECs, of which 12 EC members were affiliated with more than one EC, hence, the number of ECs represented was more, but the EC members were asked to give response for the EC which had reviewed COVID-19-related projects. These ECs were located in different States, namely Chhattisgarh, West Bengal, Odisha, Maharashtra, Karnataka, Tamil Nadu, Delhi, Uttar Pradesh and Uttarakhand.

Difficulty score for ethics committee (EC) functioning during COVID-19 pandemic: Table presents the comparison of mean difficulty scores between the groups formed on the basis of demographic characteristics, work experience, workload, and technology practices during the pandemic. The point-biserial correlation coefficients and their 95 per cent confidence intervals were generated. No significant correlation was found between difficulty scores and demographic or experiential background. The role of the respondents in EC and educational qualifications did not show any difference between the mean difficulty scores.

Reasons for choosing a difficulty score: The reasons cited for higher difficulty scores were mainly related to technical issues, pressure for expedited review with limited available information on investigational products (IPs), a large number of protocols for review, lack of hard copies, scheduling of meetings clashing with COVID duties, non-availability of staff and EC members, lockdown restrictions, difficult communication mode and internet connectivity. On the other hand, the lower difficulty scores featured the reasons such as prior proper planning of meetings, smooth handling of online meetings, quick adaptation to online formats and relative ease in organizing and participating in virtual meetings (Fig. 1).

Change in the review process before and after the COVID-19 pandemic: Most (95%) of the EC members, participating in an online survey, adopted digitalized mode of review process during the COVID-19 pandemic. However, more than one third (37%) of the respondents reported that adapting digitalized process was difficult. The most common issues raised were technical in nature pertaining to network connectivity, a sudden breach in communication and frequent interruptions in audio-video pairing (20; 67%), sharing of files (6; 21%) followed by lack of face-to-face interaction, in-person discussion and communication problems with the researchers (26%). A few EC members expressed their inability to mark comments on digital files, and loss of the same by coordinators, which they had informed and confirmed telephonically later.

However, the majority of the online survey respondents quickly adapted to the digitalized process by getting broadband connections and 56 per cent were of the opinion that the digital platform had additional advantages as it was less time-consuming as they did not have to travel, could attend meetings from home or workplace and was easier to organize. The Serious Adverse Events (SAE) Causality Analysis subcommittee meetings were also held virtually by 66 per cent of the EC members in addition to email communications (8; 27%).

Challenges reported by online quantitative survey participants: More than half of the participants reported that the submission of new and non-COVID projects reduced in number and many of the ongoing projects were halted or prematurely terminated. An increased number of missed visits by enrolled research participants were noticed by about one-third of our respondents, which ultimately led to the filing of a greater number of protocol deviations. Five (16.7%) of our respondents could not get much information about IPs as it was not available with newer drugs tried as part of COVID management. One of the participants mentioned that this situation affected the decision-making process for causality analysis.

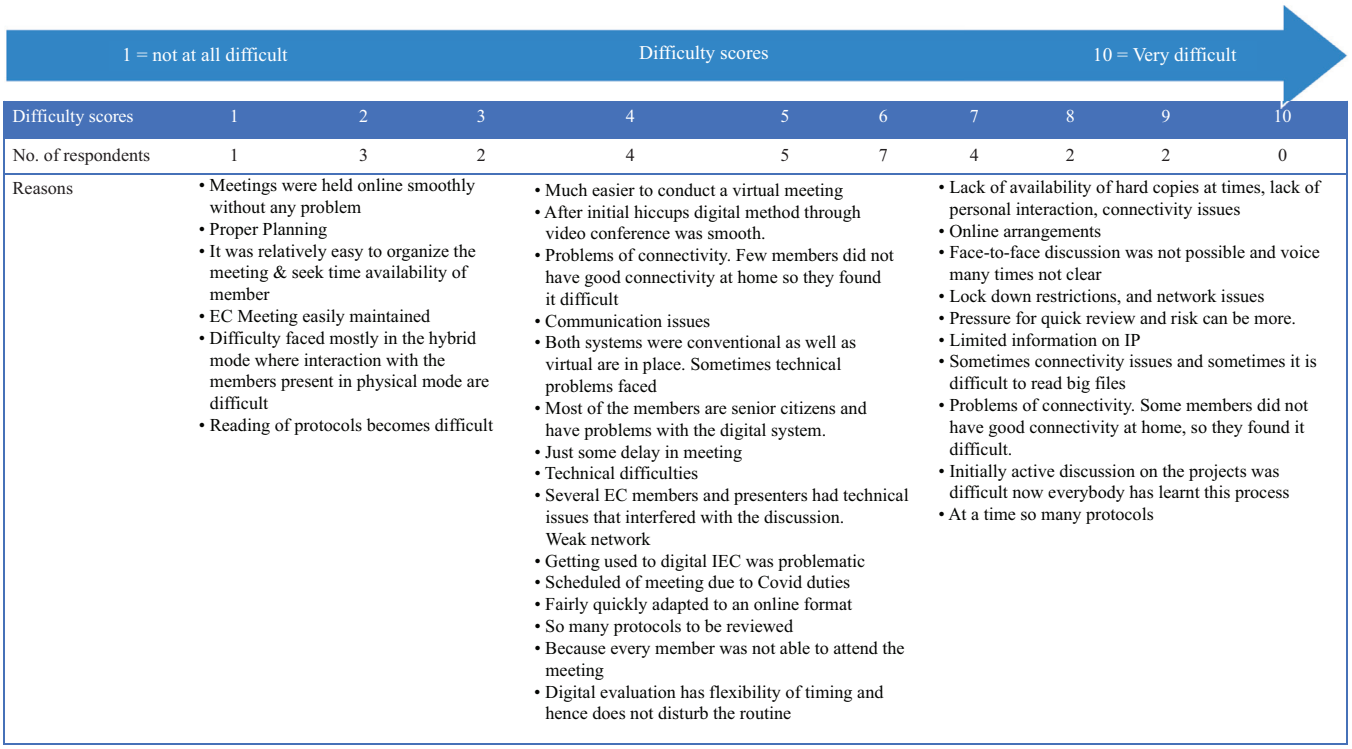
Ethical issues reported by committee members participating in an online survey: About a third of the EC members felt pressurized to provide expedited approvals and review a greater number of protocols during the pandemic situation. Moreover, they also mentioned the non-existence of a clause in their respective standard operating procedures (SOPs) to deal with the research review process in an emergency situation. Reporting of SAEs and causality analysis was delayed as mentioned by 13 per cent (4/30) of our respondents. One third of the participants reported that onsite monitoring of research projects could not take place due to COVID-related restrictions on movement. Thirty per cent (9/30) of the online survey respondents also raised concerns over not achieving a full quorum.

Table. Summary statistics of responses received through online data from ethics committees members in the survey

Characteristic	Number of individuals, n (%)	Average difficulty score (SD)	*P*	Pearson's point-biserial correlation, *r* (95% CI)
Gender				
Female	10 (33)	4.9 (2.1)	0.505	−0.13 (−0.45-0.24)
Male	20 (66)	5.45 (2.1)		
Location				
Metro cities	09 (30)	5.9 (2.1)	0.292	−0.199 (−0.499-0.17)
Other cities	21 (70)	5.0 (2.1)		
Work experience				
≤8 yr	18 (60)	5.2 (1.95)	0.889	−0.03 (−0.37-0.33)
>8 yr	12 (40)	5.3 (2.3)		
Number of expedited protocols reviewed during lockdown				
Below 10	10 (33)	5.1 (1.9)	0.763	−0.06 (−0.39-0.299)
Above 10	20 (67)	5.35 (2.2)		
Adapted digitization recently				
Yes	22 (73)	5.4 (2.3)	0.680	−0.08 (−0.41-0.28)
No	8 (27)	5.0 (1.5)		
Number of ECs affiliated with				
One	18 (60)	5.3 (2.0)	0.972	0.01 (−0.34-0.35)
More than one	12 (40)	5.3 (2.3)		
Role in EC				
Chairperson/Member Secretary	10 (33)	4.8 (1.9)	0.104	Not applicable
Basic medical scientist/clinician	10 (33)	6.4 (1.4)		
Social scientist/legal expert/layperson	10 (33)	4.6 (2.4)		
Experienced difference between the EC activities during 1st and 2nd COVID wave				
No	17 (57)	5.1 (2.2)	0.662	0.08 (−0.28-0.41)
Yes	13 (43)	5.5 (2.0)		

SD, standard deviation; CI, confidence interval; EC, ethics committees

Practiced and proposed solutions: Amendments in the existing SOPs were reported by 14 (47%) EC members followed by the usage of an online platform for meetings using ICMR guidelines for Ethics in the COVID-19 pandemic released in April 2020. Waiver of the consent process for the consenting procedure was reported by six (20%) of the EC members considering the difficulty in a physical meeting, emergency situation, potential infectiousness of the participants, retrospective analysis, risk-benefit analysis approach, and non-intervention studies. Consent to be obtained from relatives of the COVID patients was also suggested as one of the solutions by some of the EC members. Obtaining consent by using a virtual platform and getting verbal consent in the prevailing situation were found appropriate by one third (11; 33%) of the EC members and abbreviated consent was suggested by about a tenth of the respondents (4; 13.3%). Regarding vaccine trials and studies where re-purposed drugs were used, it was ensured that the participant information sheet (PIS) and informed consent form (ICF) covered such aspects. Reportedly, most of the SAE Causality Analysis subcommittees met virtually (18; 60%) for ongoing and new studies while 27 per cent (8/30) had carried out causality analysis through email communications. Protocol amendments in the form of decreased number of physical visits, telephonic investigation at sub-sites and study drug delivery by in-person or through courier were allowed by more than 70 per cent of the EC members.



Difficulty scores	1	2	3	4	5	6	7	8	9	10
No. of respondents	1	3	2	4	5	7	4	2	2	0
Reasons	• Meetings were held online smoothly without any problem • Proper Planning • It was relatively easy to organize the meeting & seek time availability of member • EC Meeting easily maintained • Difficulty faced mostly in the hybrid mode where interaction with the members present in physical mode are difficult • Reading of protocols becomes difficult			• Much easier to conduct a virtual meeting • After initial hiccups digital method through video conference was smooth. • Problems of connectivity. Few members did not have good connectivity at home so they found it difficult • Communication issues • Both systems were conventional as well as virtual are in place. Sometimes technical problems faced • Most of the members are senior citizens and have problems with the digital system. • Just some delay in meeting • Technical difficulties • Several EC members and presenters had technical issues that interfered with the discussion. Weak network • Getting used to digital IEC was problematic • Scheduled of meeting due to Covid duties • Fairly quickly adapted to an online format • So many protocols to be reviewed • Because every member was not able to attend the meeting • Digital evaluation has flexibility of timing and hence does not disturb the routine			• Lack of availability of hard copies at times, lack of personal interaction, connectivity issues • Online arrangements • Face-to-face discussion was not possible and voice many times not clear • Lock down restrictions, and network issues • Pressure for quick review and risk can be more. • Limited information on IP • Sometimes connectivity issues and sometimes it is difficult to read big files • Problems of connectivity. Some members did not have good connectivity at home, so they found it difficult. • Initially active discussion on the projects was difficult now everybody has learnt this process • At a time so many protocols		

Fig. 1. Difficulty scores for Ethics Committee (EC) functioning during COVID-19 and reasons for the score given by EC members.

Profile of in-depth interview (IDI) participants: Four of the IDI participants were chairpersons, two clinicians, one social scientist, one legal expert, one EC coordinator and one layperson. Eight IDI participants were males and two females. These members belonged to different ECs of government (3), autonomous institute (1), private medical colleges (3) and private hospitals (3) from the East, South and West regions of India. The median age of the interviewees was 59.5 yr (minimum: 39 yr and maximum: 71 yr). The time required for the completion of one IDI was about 45 min.

Findings from qualitative investigation:

Functioning through a virtual platform: During the COVID-19 pandemic, there was a sudden increase in workload as a greater number of proposals were submitted for ethical review compared to the pre-COVID era. A sense of urgency and pressure was felt by most of them to grant approvals to the proposed research work and that too in an expedited manner. Earlier ECs did not have a standard operating procedure (SOP) to deal with such an emergency. The EC members were not therefore aware of how to deal with such an event. All the interviewees mentioned that the protocols were circulated by email and were discussed in a full board meeting conducted either online or hybrid mode as recommended by ICMR guidelines[3]. The frequency of EC meetings also went down drastically initially till they adopted digitalized functioning.

'Pressure on research organizations was so much... protocols were flowing like anything… the meeting, which would have been ended in about 3 h went almost for a day. Giving expedited review without (in person) meeting was unusual...it never happened before even for expedited review'.

-Male, Member

The EC members were not comfortable with this shift to a virtual mode of functioning; most of them were not used to it. Many were not tech-savvy. The majority stated that the new norm lacked face-to-face interactions. Moreover, clarifications on issues from investigators were not always possible through this way of functioning.

'Disadvantage is - you don't meet in person… I mean that disadvantage of not being able to see nonverbal cues that the person might give… making sure that all voices are heard during the decision making… was difficult. For virtual meetings it is important to have a strong Chairperson or Member Secretory to make sure

that the rights, safety, and well-being of the patients are protected…that should not be compromised'.

-Female, Chairperson

However, a few of the in-depth interviewees welcomed this change, stating that it was time saving, convenient, quicker and above all reduced travel related hassles. Many of the members underlined the need to continue this mode of functioning in the future as well. One of the members mentioned that this actually helped lay persons to freely express themselves.

'It reduced the time for approvals... it gave me an opportunity to read the protocol at our convenience, may be at my office or at my home; so, hastened the process of approval'.

-Male, Member

'It's very important to accept the change…we have to be prepared for this kind of thing (virtual meetings) ... we were used to paper and pen procedure earlier'.

-Female, Member

One of the EC coordinators had problems related to payment of honorarium during virtual meetings as cash and cheques could not be handed over and a few EC members were not ready for online payments, but the institute heads helped in overcoming this hurdle by allowing staff to deliver honorarium to the residence of the concerned EC member following all COVID-19 appropriate precautions; receipts were collected as appropriate for audit purposes as well as official records.

Signing of conflict of interest form by EC members and signing of approval letters by EC chairperson during the lockdown in the face of the risk of transmission through fomites also posed difficulty. This was managed by voluntary logging out of the meeting during discussion and recording of the same by the EC Secretary.

Project specific issues and issues related to EC activities: Many of the projects came to a halt, especially non-COVID projects due to the lockdown situation that disabled the enrolment of study participants. Enrolled participants missed their scheduled visits as well. Many of them could not get their IPs/drugs.

'In short, it was like...our hands and legs were tied and we wanted to swim but we had not enough freedom for it…that's why projects are still pending'.

-Male, Member

However, planned protocol deviations and notes to files were saved by investigators for missed visits. Interestingly, in some cases, IPs were sent through couriers. Local physicians were asked to assess patients. Tele-consultations and follow up visits were also carried out by deploying such innovations.

Site monitoring visits by EC members could not take place. SAE timelines were missed by investigators as study participants' data were not available. Appropriate causality assessments also could not be conducted by investigators as well as EC members. However, after going through risk-benefit analyses, many of ECs laid trust in the investigators and allowed the continuation of the study in the interest of the participants.

An appropriate consenting process could not be followed in some COVID situations, where patients were participants. Alternate ways of consenting such as consenting with the help of a legally authorized representative, undertaking by the investigator or treating physician, who was not related to the study, were resorted to. In some cases, smaller subcommittees were formed, which visited sites to facilitate the process of giving approvals. One of the clinical pharmacologists who served as a chairperson for two ECs raised concerns over the consenting process during the COVID-19 pandemic of the trial participants.

'Are the patients' rights, safety and wellbeing adequately protected ...you should ask this question to yourself…a doctor is in personal protective equipment (PPE) and there is no (proper) eye contact... or is it desperation to sign a consent form… I always wondered…did the patient truly understand what was going on or were these therapeutic misconceptions... you think you are going to get better not realizing that drugs are actually repurposed'.

-Female, Chairperson

A few of the interviewees raised concerns about the quality of post-graduate dissertations.

'Ideal topic and guide were not available for post-graduate students...choice of topic or quality of research might have suffered...postgraduate students were not in a position to handle all these as they were busy in COVID duties... during the 2nd wave the ECs were more confident to carry out EC activities... however the quality of research got affected'.

-Male, Member

A few EC members talked about the efforts put up by the EC member secretary and support staff as they themselves were affected equally by COVID-19 and lockdown related restrictions.

'Truly speaking… the back-office support staff… there is no compensation for them or no honorarium for them, but they do most of the job… it is too much for a member secretary to actually handle all the projects and do all the paper works'.

-Male, Chairperson

Suggestions/solutions: Despite certain limitations, problems, and deviations during the conduct of the studies, ECs undertook due precautions or resorted to modified ways to maintain the scientific and ethical rigor of the research projects. Different suggestions/solutions were put forth by EC members for the aforementioned problems. They underlined the need for amendments in the guidelines to deal with emergency situations such as COVID, which would comprise the virtual mode of functioning of ECs, and their monitoring activities. Site operating procedures were also considered requiring changes accordingly. Many of the in-depth interviewees underscored the importance of regular training of EC members to be able to respond to the changing demand for functioning. A few EC members informed about the formation of subcommittees for expedited review with appropriate members for research related to laboratory diagnostics, socio-behavioural issues and epidemiological studies and when potential risks resulting from the proposed research were less than minimum.

'Ethics should not block the research'.

-Male, EC Chairperson

Chairpersons and members with basic medical science background mentioned that they did not have enough literature to consult before considering approval. Hence, they sent back the proposals for detailed justification and rationale for the study objectives and it was ensured that the consent forms covered such aspects.

'Mainly for vaccine protocol, there was no previous data available…this was not compromise on ethical part because everything was informed to participant through consent form'.

-Male, Member

This study is a preliminary investigation in which we have juxtaposed the findings of the quantitative and qualitative component of inquiries for synthesizing inferences. This also helped us in encapsulating the challenges faced and solutions proposed by the EC members during the COVID-19 pandemic in India and presenting them schematically in Fig. 2.

Discussion

The current preliminary study highlights some of the important issues around functioning of the ECs to ensure the conduct of principled research, during humanitarian emergency situations such as COVID-19. Urge for finding out newer drugs, developing vaccines and the need for identifying easy diagnostic techniques resulted in surges of scientific protocols, which ultimately affected functioning of the ECs. Various issues were faced by them in view of this unprecedented situation such as difficulties in adopting a virtual way of operating, the extra load of proposals to be examined, lack of site monitoring and inadequate SAE reporting. Projects, during implementation, suffered in terms of non-recruitment, missed visits by study participants and difficulties in obtaining consent. The present investigation revealed that during such a difficult time, many of the ECs in India came up with some logical and practical measures to overcome the hurdles faced such as alternate methods of consenting (virtual, abbreviated), a detailed explanation of the protocol, IPs, benefits versus risk assessment and ensuring that this is reflected in the consent, especially for vaccine trials. The longer duration and increased number of virtual EC meetings with full quorum to discuss the protocols were also reported following the circulation of protocols by email and preliminary examination.

Smaller sample size and non-diligent responses, however, imposed major limitations on this study, which was conducted as a preliminary investigation. Similar difficulties have been reported by other researchers conducting online surveys among healthcare professionals[7,8]. Unavailability of contact details of EC members was a major hurdle against our efforts to maximize our reach to all the ECs functioning during the COVID-19 pandemic in India. However, the mixed-methods approach of having in-depth qualitative interviews helped us partly in plugging such weaknesses by collating in-depth insights into the domains explored. The limitation, which, however, could not be overcome, was related to a lack of exploration around participation of pregnant women in COVID-19-related research studies.

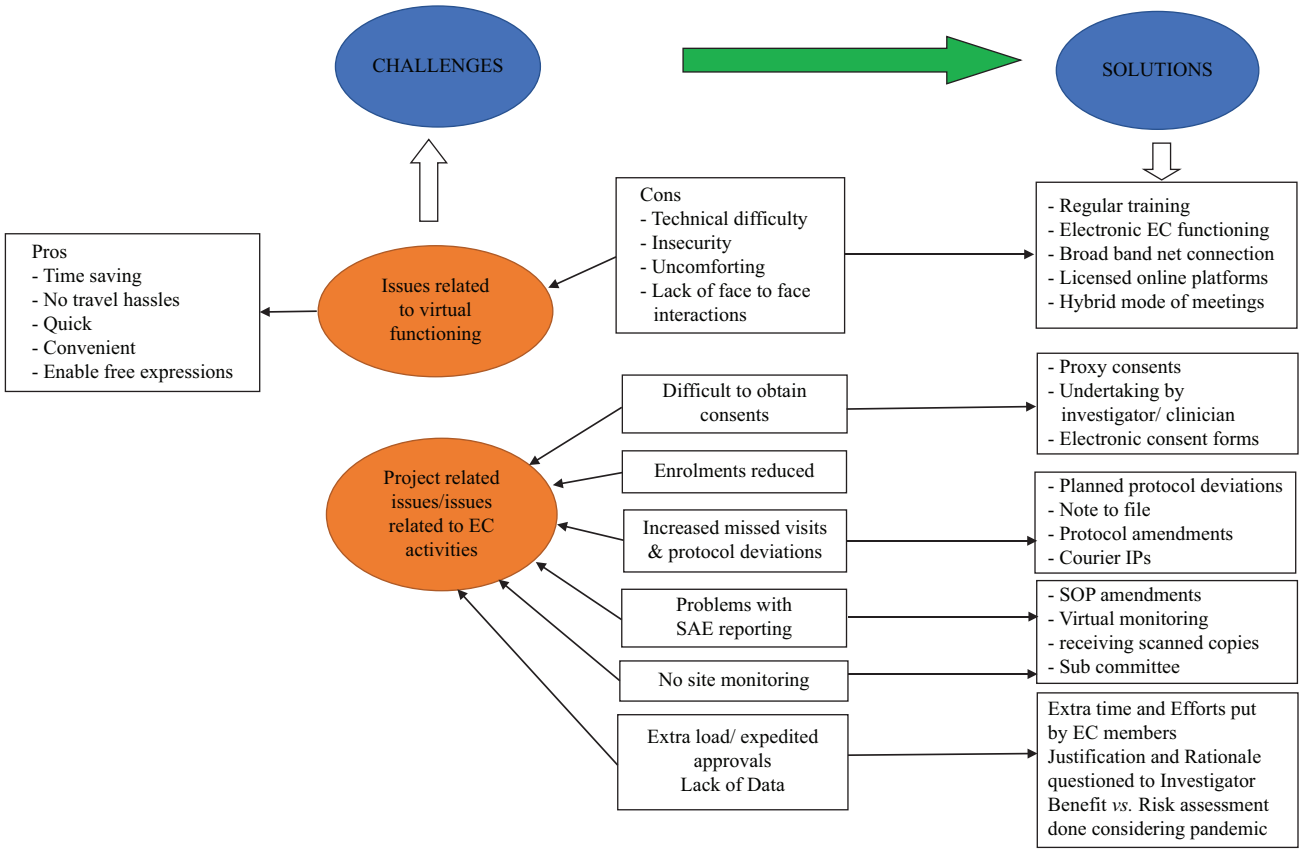


Fig. 2. Challenges faced and solutions adopted during COVID-19 by EC.

An online opinion survey conducted in India[9] reported that one fourth of the respondents had expressed difficulty in playing their respective roles through the virtual mode. We recorded a similar proportion (27%) of respondents experiencing such difficulties. The reasons for choosing high difficulty scores did not seem to follow a uniform pattern among our study participants. However, technical issues were featured most frequently.

The circulation of research proposals through emails and obtaining approvals via online platforms was perceived as controversial at the start of the pandemic while fear of lack of reliability and breach of confidentiality loomed large[10]. Licensed copies of online platforms provided some relief in this regard. Many of the EC members in the present investigation adopted a virtual mode of functioning and were comfortable joining meetings through this newer mode of communication. Similar experiences were recorded by the investigators of a study conducted among the EC members of a research institute in Chennai[11].

The EC members in the current study, during IDIs, had raised concerns about deviations in SAE timelines, which was also mentioned by about a fifth of the respondents in a survey conducted among investigators from Mumbai during the pre-pandemic period of 2016 to 2017[12]. In our study, some of the respondents expressed anxiety over limited availability of information about IPs, which led to difficulty in assessing benefits versus risks for the study participants. However, a study among EC members in China[13] recorded that although the risks were perceived to be potentially more to the individual participants, the long-term benefits to the society at large were considered greater. Although the pressure for issuance of quick approvals was felt and expressed as a need of the pandemic time, it was not perceived as political pressure as reported in the investigations conducted in other countries[14,15].

Approving the consenting process in the intensive care unit with PPE for participation in clinical trials with new drugs was a challenge faced by the EC members participating in our investigation. This was addressed by the approval of a process that would ensure video consent from patients or consent from legally acceptable or authorized representatives whenever possible, which

was similar to the findings from studies conducted in Germany[16]. Waivers for consent were given only for secondary data analysis, retrospective studies and laboratory studies where leftover samples were used following de-identification[17]. The EC members were more confident to carry out EC activities during the second wave (taking off in February 2021 and attaining its peak during March 2021) than the time around the first wave (taking off in April 2020 and attaining its peak in September 2020); 47 per cent of the EC members did not report any changes in EC functioning.

Non-COVID projects, requiring fieldwork, and projects where sample collection or interventions were necessary, were halted and there was a distinct drop in the number of non-COVID projects as a result of prioritizing COVID-19 research applications. Similar issues were reported from other countries, such as China, which were hit hard by COVID-19[18,19].

As post-graduate students were deployed in COVID duties[20], they could not dedicate full time to their thesis work, nor could they follow the participant enrolment process as per their own thesis protocol. At times, their thesis topics were changed to systematic reviews and pharmacovigilance studies. This emerged as a noteworthy finding during IDIs in our investigation. EC members extended help to the post-graduate students by advising them to change their topics or by modifying the study designs. Researchers identifying similar issues raised concerns as the execution of a planned thesis/dissertation is viewed as a quintessential step towards learning basic research methodology[21]. EC members supported researchers by advising them to file planned protocol deviations or allowing telephonic follow up in case of missed visits by participants and allowing delivery of IPs through courier services.

Certain safety concerns such as no site monitoring visits, missing of SAE timelines by investigators and lack of proper causality assessments were also raised. However, ECs allowed the continuation of the study in the interest of participants after going through the risk–benefit considerations. In contrast, London and Kimmelman[22] mentioned the importance of rigorousness in the methods. They further emphasized that the pandemics should heighten the responsibility of ECs to coordinate their activities and to uphold the standards necessary.

The timely release of ICMR guidelines along with SOP for COVID research proved useful for the majority of the EC members. Prior approvals from the Central EC for Human Research of the ICMR helped the site-specific EC in providing approvals for projects, especially related to laboratory diagnostics as there was increasing demand for evaluation of a large number of alternate diagnostic kits during the COVID-19 pandemic[23]. One of the solutions, as stated by a few EC members, was forming smaller sub-committees and online reviews through emails or virtual meetings to provide expedited approvals. A study by IJKema *et al*[24] recorded a median review time of 10.5 days, and similar approaches for approvals on an urgent basis were adopted by ECs in The Netherlands.

There was a consensus among EC members about balancing the duty of protecting individual participants *vis-a-vis* special public health needs related to pandemic control. There was recognition by most of the respondents about the need for maintaining ethical principles of autonomy, beneficence, non-maleficence and justice. Similar opinions were expressed by the EC members in the study by Monaco *et al*[25].

However, a few EC members expected more regulatory support and relaxation in case of unintentional delays and mistakes, application of ethical principles in a more flexible manner and making the procedures simpler to achieve streamlining as the pandemic in concern was a shocking and sudden experience for everyone. This was expressed by EC members in other investigations as well[19].

Overall, this mixed-methods study provided an in-depth understanding of various concerns and issues faced by the EC members from different ECs across India. A larger study is, however, needed to capture the experiences of a wide range of EC members, encompassing difficulties expressed and the solutions found. Our study underlines that the challenges related to EC functioning during a humanitarian crisis such as COVID-19 can be dealt with appropriate innovation. Biomedical research projects aiming to conduct rapid socio-epidemiologic investigations during a newly emerging public health crisis such as Ebola, Nipah or COVID-19 outbreak and identify preventive interventions, diagnostic and therapeutic measures would be heavily dependent on such innovation that would help strike a balance between ethics and urgency.

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References

1. Kumar NK, Muthuswamy V. Fostering ethical biomedical and health research in India during the COVID-19 pandemic. *Res Ethics* 2020; *16* : 1-10.
2. Indian Council of Medical Research. *National ethical guidelines for biomedical and health research involving human participants*.. Available from: *https://main.icmr.nic.in/sites/default/files/guidelines/ICMR_Ethical_Guidelines_2017.pdf*, accessed on November 13, 2020.
3. Indian Council of Medical Research. *National guidelines for ethics committees reviewing biomedical and health research*. Available from: *https://main.icmr.nic.in/sites/default/files/guidelines/EC_Guidance_COVID19_06_05_2020.pdf*, accessed on November 13, 2020.
4. Bavdekar SB. Ethics committees: Actions during pandemic and lockdown situations. *J Postgrad Med* 2020; *66* : 119-22.
5. Mathur R. Ethics preparedness for infectious disease outbreaks research in India: A case for novel coronavirus disease 2019. *Indian J Med Res* 2020; *151* : 124-31.
6. Park JW, Jung MS. A note on determination of sample size for a Likert Scale. *Commun Stat Appl Methods* 2009; *16* : 669-73.
7. Kulkarni R, Prusty RK, Chakma T, Thomas B, Menon GR, Singh R, *et al*. Challenges and opportunities in mixed method data collection on mental health issues of health care workers during COVID-19 pandemic in India. *Int J Res Med Sci* 2022; *10* : 838-44.
8. Hutchinson MK, Sutherland MA. Conducting surveys with multidisciplinary health care providers: Current challenges and creative approaches to sampling, recruitment, and data collection. *Res Nurs Health* 2019; *42* : 458-66.
9. Mukherjee S, Samajdar SS, Tripathi R, Tripathi SK. Functioning of institutional ethics committees during the COVID-19 pandemic: An opinion survey. *Perspect Clin Res* 2022; *13* : 118-9.
10. Ghooi RB. Ethics committee meetings – Online or face to face? *Perspect Clin Res* 2020; *11* : 121-3.
11. Poongothai S, Aarthy R, Lalasa M, Viswanathan K, Mohan V. Virtual ethics committee meeting during the COVID-associated lockdown – Madras Diabetes Research Foundation Experience. *Perspect Clin Res* 2022; *13* : 60-1.
12. Figer B, Gogtay NJ, Thatte UM. Compliance of Mumbai-based clinical trial sites with the Quality Council of India guidelines and evaluation of the challenges faced by the investigators. *Perspect Clin Res* 2021; *12* : 133-9.
13. Pan Z, Chu H, Zhang Y, Hong X, Liang L, Zhao W, *et al.* Perspectives of research ethics committee members on human challenge studies in the development of vaccines against COVID-19: A mixed methods study. *Ann Palliat Med* 2021; *10* : 6259-69.
14. Shekhani S, Iqbal S, Jafarey A. Adapting the ethical review process for COVID-19 research: Reviewers' perspectives from Pakistan. *East Mediterr Health J* 2021; *27* : 1045-51.
15. Ekmekci PE, Güner MD, Buruk B, Güneş B, Arda B, Görkey Ş. Challenges and practices arising during public health emergencies: A qualitative survey on ethics committees. *Dev World Bioeth* 2022. DOI:https://doi.org/10.1111/dewb.12345.
16. Faust A, Sierawska A, Krüger K, Wisgalla A, Hasford J, Strech D. Challenges and proposed solutions in making clinical research on COVID-19 ethical: A status quo analysis across German research ethics committees. *BMC Med Ethics* 2021; *22* : 96.
17. Um T, Nj G. Research and ethics during the COVID-19 pandemic. *J Assoc Physicians India* 2020; *68* : 11-2.
18. Zhang H, Shao F, Gu J, Li L, Wang Y. Ethics committee reviews of applications for research studies at 1 hospital in China during the 2019 novel coronavirus epidemic. *JAMA* 2020; *323* : 1844-6.
19. Ma X, Wang Y, Gao T, He Q, He Y, Yue R, *et al.* Challenges and strategies to research ethics in conducting COVID-19 research. *J Evid Based Med* 2020; *13* : 173-7.
20. Patil A, Ranjan R, Kumar P, Narang H. Impact of COVID-19 pandemic on post-graduate medical education and training in India: Lessons learned and opportunities offered. *Adv Med Educ Pract* 2021; *12* : 809-16.
21. Dwivedi R, Kumar R. Postgraduate training requires urgent reforms to deal with future pandemics. *J R Coll Physicians Edinb* 2020; *50* : 360-1.
22. London AJ, Kimmelman J. Against pandemic research exceptionalism. *Science* 2020; *368* : 476-7.
23. Jayaprakasam M, Aggarwal S, Mane A, Saxena V, Rao A, Bandopadhyay B, *et al*. RNA-extraction-free diagnostic method to detect SARS-CoV-2: An assessment from two states, India. *Epidemiol Infect* 2021; *149* : E245.
24. IJkema R, Janssens MJPA, van der Post JAM, Licht CM. Ethical review of COVID-19 research in the Netherlands; a mixed-method evaluation among medical research ethics committees and investigators. *PLoS One* 2021; *16* : e0255040.
25. Monaco E, Pisano L, Nasato L, Lorenzoni G, Gregori D, Martinato M. Ethics committees in the time of COVID-19. *Epidemiol Prev* 2020; *44* : 113-8.

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Annexure 1

ICMR-National AIDS Research Institute, Pune

Challenges faced by Ethics Committee members and the solutions found for resolving them during COVID-19 Lockdown: A Telephonic/Online Survey

Instructions-

1) Questionnaire comprises total eight sections.
2) You can opt multiple answers.
3) It will take 10-20 minutes.
4) Participant information sheet and consent form are attached with the email for your kind reference.

* Required

General Information (I)-Section '1 of 8'

1. City

   _____

2. How old are you?- _____ Age in completed years)

   _____

3. Gender :

   Mark only one oval.

   ◯ Male
   ◯ Female
   ◯ Other: _____

4. a) How many ECs are you affliated with? Please mention your roles in various * Ethics Committees? (Please don't mention name of ECs to maintain confidentiality)

   _____

   _____

   _____

   _____

   _____

   b) The ethics committees you are associated with belong to which sector(You can select multiple options if any)

   Check all that apply.

- ◯ Government Setup
- ◯ Private Setup
- ◯ Dependent
- ◯ Independent
- ◯ Other: _____

5. What is your educational qualification?

   _____

6. Work experience with Ethics Committee (In Years)?

   _____

7. a) Are you willing to participate in the study. *

   Mark only one oval.

   - ◯ Yes
   - ◯ No

   Reason for unwillingness of participation in the survey-Section '1 of 8'

   b) If no, reasons for no participation to continue(not mandatory to respond to this question)

   Check all that apply.

   - ◯ Not enough time
   - ◯ Lack of interest
   - ◯ Privacy issues
   - ◯ Unwillingness to disclose information
   - ◯ Do not prefer to answer
   - ◯ Other: _____

   c) If you want to discontinue please confirm by clicking yes.

   Mark only one oval.

   - ◯ Yes
   - ◯ No

   General Information (II)-Section '1 of 8'

8. Review process prior to COVID 19

   Mark only one oval.

   - ◯ Digitalized Process
   - ◯ Conventional Process
   - ◯ Mixture of both

9. Review process during COVID-19?

   Mark only one oval.

- ◯ Digitalized Process
- ◯ Conventional Process
- ◯ Mixture of Both

10. How many protocols/studies were reviewed by you during COVID-19 lockdown approx.?

    Mark only one oval.

    - ◯ <5
    - ◯ 6-10
    - ◯ >10

11. How many protocols/studies were reviewed by you for expedited approval?

    Mark only one oval.

    - ◯ <5
    - ◯ 6-10
    - ◯ >10

Challenges Faced-Section '2 of 8'

12. Please look at the Visual Analogue Scale and mark a point on it to capture * the diffculty level in the functioning/arrangement of EC activities in the COVID pandemic situations.

    Mark only one oval.

	1	2	3	4	5	6	7	8	9	10	
Not at all difficult	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	Extremely Difficult

13. What were the reasons for the choice of your score?

_____

_____

_____

_____

_____

14. What were the major challenges (Technical, Scientific, Logistic, Ethical, Staff and any other) faced pertaining to EC functioning during COVID-19 situation and how they were dealt?

_____

_____

_____

_____

_____

15. What were the minor challenges (Technical, Scientific, Logistic, Ethical, Staff and any other) faced pertaining to EC functioning during COVID-19 situation and how they were dealt?

_____

_____

_____

_____

_____

16. What were the guidelines referred during this pandemic?

_____

_____

_____

_____

_____

17. Did you experience any pressure to have an expedited review which could led to compromises in the ethical conduct of the study?

Mark only one oval.

- ◯ Yes
- ◯ No

18. Whether any of the below EC activity was postponed or cancelled?

Check all that apply.

- ◯ On-Site monitoring
- ◯ Monitoring Supervision
- ◯ Physical Meeting
- ◯ Training
- ◯ Other: _____

19. Were there any communication Challenges with EC members/researchers during this situation?

Mark only one oval.

- ◯ Yes
- ◯ No

20. Was it diffcult for achieving full quorum?

Mark only one oval.

- ◯ Yes
- ◯ No

21. What was the difference between the EC activities during 1st COVID wave and 2nd COVID wave?

_____

_____

_____

_____

_____

Virtual EC Meeting Issues-Section '3 of 8'

22. What were the most common issues faced by you during meeting?

Check all that apply.

- ◯ Disconnections due to internet issues
- ◯ Audio video Challenges
- ◯ Issues related to sharing of files
- ◯ Other: _____

23. Were you comfortable with digitalized (virtual) functioning?

Mark only one oval.

- ◯ Yes
- ◯ No

24. Do you think digital processing gave an additional advantage?

Mark only one oval.

- ◯ Yes
- ◯ No

EC-SOPs Related-Section '4 of 8'

25. Did your SOP have any clause to deal with review during emergencies/pandemics/Expedited review prior to COVID-19?

Mark only one oval.

- ◯ Yes
- ◯ No

26. a) Did you make any amendments in the existing SOP?

Mark only one oval.

- ◯ Yes
- ◯ No

b) If Yes, Please enumerate

_____

_____

_____

_____

_____

27. a) Were there any changes made in decision-making processes pertaining to approvals for the projects?

Mark only one oval.

- ◯ Yes
- ◯ No

b) If yes, please specify.

_____

COVID Pandemic Affecting the Studies-Section '5 of 8'

28. a) Did COVID-19 have any effect on any project?

Mark only one oval.

- ◯ Yes
- ◯ No

b) If Yes, Please elaborate

_____

_____

_____

_____

_____

29. Did COVID-19 affect submission of new projects?

Mark only one oval.

- ◯ Yes
- ◯ No

30. a) Whether there were any requests for protocol amendments of ongoing studies?

Mark only one oval.

- ◯ Yes
- ◯ No

b) If yes, what type of protocol amendments were requested?

Check all that apply.

- ◯ Telephonic calls instead of actual visits
- ◯ Decreased no. of personal visits
- ◯ Courier-based study drugs delivery
- ◯ Investigations done at sub-sites
- ◯ Other: _____

31. Were any protocol deviations/violations reported during this period?

Check all that apply.

- ◯ Telephonic safety follow up
- ◯ Home dispensing or Dispensing through courier?
- ◯ Missed visits
- ◯ No Deviations/Violations reported
- ◯ Other: _____

32. How were those protocol deviations/violations dealt with?

_____

_____

_____

_____

_____

33. Was any of the site or project closed/halted due to COVID-19?

Mark only one oval.

- ◯ Yes
- ◯ No

34. Whether the review of new non-COVID related research limited?

Mark only one oval.

- ◯ Yes
- ◯ No

COVID Pandemic Affecting the Consent and Consent Process-Section ‘6 of 8’

35. Consent and Consent process...

a) Was there any waiver given for consent process?

Mark only one oval.

- ◯ Yes
- ◯ No

b) If yes, what was basis for giving waiver…..

_____

_____

_____

_____

_____

36. Please specify if any alternatives for the consent given from below-

Check all that apply.

- ◯ Abbreviated consent
- ◯ Video verbal consent
- ◯ Virtual consented
- ◯ Other: _____

SAE Related EC Roles and Issues-Section '7 of 8'

37. Was there any diffculty in arranging meeting of SAE subcommittee?

Mark only one oval.

- ◯ Yes
- ◯ No

38. How did the SAE subcommittee function during COVID-19 lockdown for ongoing studies?

Check all that apply.

- ◯ Virtual Meeting
- ◯ Responses by email circulation
- ◯ Physical Meeting
- ◯ Not applicable
- ◯ Other: _____

39. Were there delays in causality analysis reporting?

Mark only one oval.

- ◯ Yes
- ◯ No

40. Did you give any relaxation for timelines for SAE reporting during COVID-19?

Mark only one oval.

- ◯ Yes
- ◯ No

41. Was there any effect on decision-making process for causality analysis?

Mark only one oval.

- Yes
- No

Suggestions-Section ‘8 of 8’

42. Any suggestion for the regulatory authorities/policymakers.

_____

_____

_____

_____

_____

Thank you for participating in the study!

Annexure 2

In-Depth Interview Guide for Study Titled "Challenges faced by Ethics Committee members and the solutions found for resolving them during COVID-19 Lockdown: A Telephonic/Online Survey"

In-Depth Interview Guide

SECTION 1: GENERAL INFORMATION

101. Site:- _____

102. Date DD MM YYYY

103. Start Time

104. Time

105. Interview: Video Conference _zoom/webex or telephone (Strike out whichever is not applicable)

Respected Sir/Madam,

My name is _____ (Name of the moderator). I will conduct your interview and keep notes in addition to recording your responses.

I would like to thank you for agreeing for video conference call-based interview using zoom or webex link platform. 'Can I seek your permission for recording of conversations by clicking on recording tab of the zoom/ cisoc webex for this interview'. This would ensure that I don't miss out on anything and play it later to listen to our conversations and learn from them?

In case interview is being conducted over telephone:

'Can I seek your permission to switch on the tape recorder for recording our conversations so that I don't miss out on anything and play it later to listen to our conversations and learn from them?'

(ENCIRCLE BELOW THE RESPONSE FOR RECORDING AS APPROPRIATE)

- Yes
- No

Start Recorder if permitted and Read Introduction:

Before I begin I would appreciate it, if you could please share something about yourself

106. Study ID No _____

107. How old are you?- _____ Age in completed years)

108. Gender M/F/OTHER

109. What is your role in the Ethics Committee? .....

110. What is your basic qualification? ----------

111. Since how long you are the member of this Ethics Committee? …….

112. How many protocols/studies were reviewed by you during COVID-19 lockdown approximately?

113. How many protocols/studies were reviewed by you for expedited approval?

SECTION 2

Ethics committee functioning during COVID-19

I would like to thank you again for accepting my invitation to participate in this study.

We are interested in knowing your views about issues that will be asked. Please note that there is no wrong or right response. If there are any apprehensions that you would like to talk about you may bring them up even if we haven't asked them. If there is any question that you would like to ask I would take a note of them and answer them after this interview. If we are unable to answer any of the questions, we would refer them to an appropriate person.

201. How comfortable were you in accepting my invitation for participation in this study?

Probes

a. Did you feel it was important for you to participate? Why?
b. What benefits do you see of participating? Why?

202. We would like to know about the functioning of your EC before COVID situation and during COVID and now?

Probes

Any difference

Any instances

Your experience with virtual platform

Merits and demerits

203. How was your experience while giving expedited review during COVID-19 situation?

Probe

The pressure to have expedited review led to compromises in the ethical conduct of the study? If yes what aspects of the ethical aspects were more likely to have been impacted?

Did you experience any compromises in the ethical conduct of the study?

If yes, please elaborate

204. Please tell us the Challenges faced by you?

(For every problem mentioned please try to elaborate in details)

Probes

Any Technical Challenges?

Bio-Medial; epidemiological, and social and behavioural studies have specific ethical challenges closely intertwined with the technical aspects of the study. For example, conceptual integrity, methodology rigour and interpretative abilities will be differentially impacted by the compromises for different types of study. It would be insightful to know how were then, they addressed

Any Scientific Challenges?

Any Logistic Challenges?

Any Ethical Challenges?

Staff issues/Challenges

205. What do you think - Any impact on ethical aspects?

Probe- please elaborate

Consent and Consent process...

Q: Was there any waiver given for consent process.. if yes what was basis for giving waiver

Q. Any alternatives for the consent ...Abbreviated consent …/Video verbal consent

/Virtual consent...

206. Did you find solution to these issues?

Please elaborate

207. May I know the solution/measures/steps taken by you to tackle the problem?

Probe-

Did you refer any guidelines? If yes, please explain…….

208. May I know any new strengths/measures/innovations developed by you to overcome these Challenges?

Probe:

209. Do you have any suggestions for regulatory authorities?