BMC Medical Ethics

RESEARCH

Open Access

Ethical challenges in conducting research in low and middle income setting during public health emergencies: a qualitative evidence of a COVID-19 pandemic: the experience of Iran

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Abstract

Background Every minute during an epidemic is important and research in such conditions is for the benefit of the society. Considering that identifying experiences is a way to prevent repeated mistakes and prepare people to face crisis situations, this study aimed to explain participants' experiences of ethical challenges encountered in conducting research related to Covid-19 in Iran.

Method This qualitative study was carried out using conventional content analysis for 2 years from March 2020 to March 2022 in Tehran, Iran. A number of 30 people were selected in a purposeful method and information was obtained through semi-structured interviews. The participants in the study were people with positions including members of institutional and national research ethics committees, researchers, clinicians, university hospitals managers during the COVID-19 pandemic. The method of data analysis in this study was conventional content analysis using the Graneheim and Lundman method.

Results Participants' experiences on ethical challenges were explained through three themes: "substantive ethical values principles", "the Research Environment", "Research Governance and Management".

Conclusion This study examines ethical challenges in COVID-19 research across three domains: values, environment, and research governance. The results suggest the need to develop crisis-specific ethical frameworks, strengthen research ethics infrastructure and training, and establish more transparent standards and oversight systems. These findings could be useful in refining ethical policies and managing future crises.

Keywords Covid-19, Emerging disease, Ethics, Iran, Research, Pandemic, Crisis

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Introduction

In December 2019, the transmission of a novel coronavirus (SARS-CoV-2) to humans was officially reported in Wuhan, the capital of Hubei Province, China. This virus rapidly escalated into a global pandemic [1–3]. While most infected individuals experienced mild to moderate respiratory symptoms and recovered without specialized treatment, some required hospitalization [4]. By end of 2024, over 800 million confirmed cases and more than seven million deaths had been reported worldwide [5]. Despite extensive research, significant evidence regarding the time, location, and mechanisms of the emergence of new diseases remains unavailable [1, 2, 6], and the fear of pandemics persists [7–9].

Pandemics have profound impacts on human societies [10], necessitating continuous demand for scientific evidence to manage challenges and control disease spread. The World Health Organization (WHO) has urged countries to conduct extensive research to accelerate the research process and establish new standards for controlling virus outbreaks and assisting in patient care [4]. However, conducting scientific research in emergency situations, such as the COVID-19 pandemic, faces numerous ethical challenges. These challenges involve the protection of society, human beings, and the environment. Although existing ethical standards have been developed within specific historical and social contexts and are generally used to assess research under normal conditions, their implementation during a pandemic, especially considering time constraints and pressure on healthcare systems, can be particularly challenging [11].

Various factors influence the complexity of conducting research during infectious disease outbreaks. For instance, frontline healthcare workers simultaneously provide diagnostic and therapeutic services while also participating in scientific research activities. In addition, streamlining research review, evaluation and implementation by Research Ethics Committees (RECs) and other stakeholders is a significant challenge [3, 12, 13].

Iran was among the first countries to face the COVID-19 outbreak after China. To date, over 7.7 million cases and approximately 150,000 deaths related to the disease have been reported in the country [6]. This pandemic has significantly impacted Iran's economic, social, and political dimensions [14]. The coincidence of parliamentary elections with the onset of the disease politicized the pandemic response from the very beginning [15]. Furthermore, the lack of effective treatments, limited access to vaccines, dissemination of misinformation, and disruption of family connections because of fear and social stigma increased the vulnerability of individuals [16]. The Iranian scientific community, like many others worldwide, responded rapidly to the pandemic by designing and implementing numerous research projects to explore various aspects of the disease. Among these, a substantial number of COVID-19-related clinical trials were registered in the Iranian Registry of Clinical Trials, highlighting the extensive focus on this area [10, 17].

According to Iranian regulations [18], all research proposals must be reviewed by RECs. Despite the presence of a national ethics review system with over 200 accredited committees, the ethical evaluation of research projects has been a significant challenge during the pandemic. In the post-COVID era, which may serve as a precursor to future pandemics, examining ethical challenges of performing research in such emergencies is essential. Such evaluations contribute to documenting lessons learned, preventing the repetition of mistakes, and preparing research ethics systems to address future health crises. While the scientific and medical challenges of COVID-related research have been the main focus of many studies, the challenges related to ethical implications of pandemics and health emergencies such the challenges faced by REC members, researches and healthcare workers of ethics review process and other issues is mostly overlooked and have gotten very little attention, specifically in Low-and-Middle-Income Countries (LMICs). By looking at the viewpoints of researchers and policymakers, qualitative research can offer a more accurate picture of these difficulties. This study aims to identify and explain participants' perceptions of the ethical challenges in COVID-19-related research in Iran, as a developing middle-income country which was seriously affected by the pandemic.

Method

A qualitative study was conducted using conventional content analysis over a two-year period, from March 2020 to March 2022, in Tehran, Iran. After obtaining ethics approval (IR.TUMS.DDRI.REC.1399.041) from the Tehran University of Medical Sciences, the research team convened to select appropriate study participants from across the country. Following the explanation of the study's objectives and methodology, participants were invited to participate in interview sessions. A purposive sampling method for participant selection was employed to ensure the collection of accurate and reliable data. Participants were selected by the research team, who were familiar with research and ethics review activities during the pandemic and had prior knowledge of some REC members and researchers. The initial list of potential participants was later expanded through recommendations from earlier participants in a snowballing manner. The predefined criteria, required them to have relevant experience in ethical review such as being members of RECs and conducting health research during the COVID-19 pandemic, including a minimum of six months experience in the field during the pandemic, and to currently

hold positions directly related to the concept under investigation.

A total of 30 in-depth, semi-structured interviews were conducted. Following explanations of the research's objectives, the incorporation of audio recordings, and securing informed consent from the participants, interviews were carried out. Most interviews (29 of the total) were conducted via an online video conferencing platform called Skyroom due to COVID-19 pandemic restrictions. One interview was conducted in person, followed by an online meeting, because the participant's extensive experiences as the secretary of NCEBR required deeper exploration, which could not be fully achieved in a single online session. "The same interview guide and probing questions were used across both face-to-face and online interviews, ensuring consistently in data collection". Data saturation was reached after 27 interviews, but to ensure thoroughness, three additional interviews were conducted. Saturation was determined through concurrent data analysis during data collection, where no new information emerged that required further exploration.

The interviews were conducted using an interview guide (Table 1). Then, by asking probing and clarifying questions, the content of each interview was designed to cover the objectives of the research. While the first question was a general question about the ethical challenges of designing, reviewing, and conducting research during the time of the pandemic, interviews continued with follow-up and exploratory questions (please explain more? What do you mean by this? Please give me an example?). Gradually, by analyzing the data and creating categories, the path of the next interviews was determined. The duration of the interviews varied from 20 to 120 min and an average of 31 min according to the conditions and interest of the participants in explaining their experiences and perceptions.

The data analysis method employed was conventional content analysis, following Graneheim and Lundman's (2004) approach [19]. The analysis began with the first interview and continued until data saturation was reached. The steps of the analysis were as follows: Immersion: The researcher developed a deep understanding of the data by carefully and repeatedly reading the collected texts. The content is organized hierarchically into Themes, Categories, Subcategories, and Units, with Themes being the most general and Units the most specific. To develop "Meaning Units" the text was divided into smaller segments, each conveying meaning relevant to the research topic. Then the meaning units were rewritten concisely to reduce the volume of data while preserving their essence to develop "Condensed Meaning Units". For "Coding", the condensed meaning units were assigned codes based on key words or phrases that reflected their content. Related or similar codes were grouped into "Subcategories", representing shared concepts. Identifying "Categories" and "Themes" was the next step. Categories were analyzed to identify overarching "Themes" or general patterns in the data. These "Themes" represent broader concepts, revealing the primary messages of the research. Finally, in a "Review and Interpretation" step, the "Subcategories", "Categories" and "Themes" were reviewed and interpreted to ensure they were accurate, coherent, and aligned with the research objectives. In this study, to enhance the credibility of the research, participants with diverse experiences were purposefully selected. The interviews were conducted in Persian, and translation and back-translation processes were indeed implemented to ensure the accuracy and reliability of the data.

The interview transcripts and extracted codes were shared with four participants, who were asked to review and provide feedback on the accuracy and precision of the material. Any discrepancies identified were thoroughly investigated, and ambiguities or misconceptions were clarified through follow-up telephone calls with the participants. For example, participants were asked to comment on whether their responses were accurately reflected in the transcripts, leading to necessary adjustments. To ensure transferability, the data were reported accurately and transparently, allowing other researchers to apply the findings in similar contexts. Dependability was reinforced through scientific auditing, during which three independent observers meticulously examined the data to verify the stability and robustness of the research process. Lastly, to ensure confirmability, which require research findings are driven by the data itself rather than being influenced by researcher bias, personal motivations, or preconceived assumptions, according to Lincoln and Guba's framework, the research methodology and implementation steps were shared with several research colleagues, who reviewed and confirmed the accuracy and reliability of the process, ensuring that the findings were not influenced by researcher bias [20].

For analyzing the results of this study, we used the general principles outlined by various international research ethics standards, including those from CIMOS. The general ethical framework includes a number of substantive ethical principles, which cover considerations from both traditional consequentialist and deontological ethical theories. In discussion substantive ethical issues including social value, autonomy and the participants' right to self-determination, participants' and other stakeholders' well-being, and equity and justice as well as procedural values such as transparency, accountability and inclusion are used as the overarching values.

Table 1 Interview guide

Prior to the interview:	Send an email to the selected participant and introduce yourself and give a brief explanation of the study and why the investigators selected them to be invited as an interviewee and ask for a time. Also, send a file consisting of a summary of the project by email. In case of non-response, send a reminder email and emphasize the importance of the interview. In case of a negative response thank the invitees and politely ask if they can explain the reason for the rejection. In case of a positive response, set a time for the interview and confirm the meeting time by sending a reminder email or SMS two days before the interview. Ensure your recording instrument before the interview. Try to be on time and attend the meeting 15 min before the time of the interview. Study title: Ethical Challenges in Conducting Research in Low and Middle Income Setting during Public Health Emergencies: A Qualitative Evidence of a COVID-19 Pandemic Participant number: Participant group (specialty): Interview date:
Duration of the interview:	To start the interview: • Ask for consent to turn the voice recorder on. Assure the participants about the confidentiality of the gathered data. • After turning on the recorder, introduce yourself, the interviewee, and the date of the interview, and seek the interviewee's consent to participate in the study and interviews. • Explain the study's objectives and justification, briefly explaining the background and defensive medicine definition and introducing the study's team. • Start questions one by one as below. • During the interview, try not to interrupt the interviewee. If the discussion goes out of the topic, try to draw back the interviewee's attention to the study's objectives. • In case the interviewees do not understand the question truly, give them examples of what is already said in literature or previous interviews. • At the end of the interview, give a brief explanation about the next steps, the transcription of interviews, and the time that the research team keeps the recorded files and ask participants to ensure they have any other comments or suggestions. • Prepare a visit card with your contact details and ask the participants to share any other issues, thoughts, or ideas with you through email. The open-ended question would be asked at the beginning of the interviews to help the participants freely share their perspectives, here are general questions: • What ethical issues did you experience in the research related to Covid? • What ethical issues did you face while reviewing the designs? • What ethical issues were associated with the implementation of research projects? • How was your experience with the media? In different participants, according to the initial answer, guided questions were asked. Also, participants were asked to give more explanations by asking for examples.

Results

A total of 30 in-depth, semi-structured interviews were conducted. 12 participants (40%) were female and 18 (60%) were male. Among the participants, 15 were affiliated with at least one REC, with three also serving on the National Committee for Ethics in Biomedical Research (NCEBR) under the Ministry of Health and Medical Education. Additionally, 26 participants had medical backgrounds and were actively involved in providing clinical care to COVID-19 patients. Three participant was a member of the National Clinical Ethics Committee under the Ministry of Health and Medical Education. Some participants held multiple roles simultaneously, as detailed in Table 2. For example, a participant might simultaneously hold roles as a researcher at one institution and as a member of the NCEBR or another REC. This is common because, according to the standard composition of RECs, several researchers are typically included as members. While the role of other positions in demonstrating the ethical challenges of COVID-19 research is evident, it is noteworthy that the hospital managers we interviewed are from university hospitals, where the majority of clinical research is conducted. Their insights were valuable for this study, as one source of ethical challenges in situations such as pandemics and public health emergencies could stem from the dual responsibilities of clinical researchers, who are both researchers and clinicians. Additionally, hospitals often serve as both treatment centers and research fields, further complicating ethical considerations.

In the analysis of the 30 interviews' content, 3430 initial codes were extracted. After merging the similar codes, 1620 codes were obtained and by merging them, 65 subcategories were finally obtained, which were categorized in 11 categories and three main themes. Each of Tables 3, 4 and 5 shows the, categories, and subcategories.

Substantive ethical values principles (Table 3)

This study participants perspectives and ethical concerns related to research in the Iranian context can be grouped into four main categories: Social Value, Autonomy and the Participants' Right to Self-Determination, Participants' and Other People's Well-being, and Justice and Equity.

Social value

There were significant concerns about the social value of research, particularly regarding the contribution of Iranian researchers and institutions to international research. One researcher highlighted the issue, stating, "In many cases, some research studies were approved that even if the results were satisfactory, it was not possible to use those interventions for the general public because of their expensive price or hard-to-access

Table 2 Participants' characteristics, qualifications, and experiences

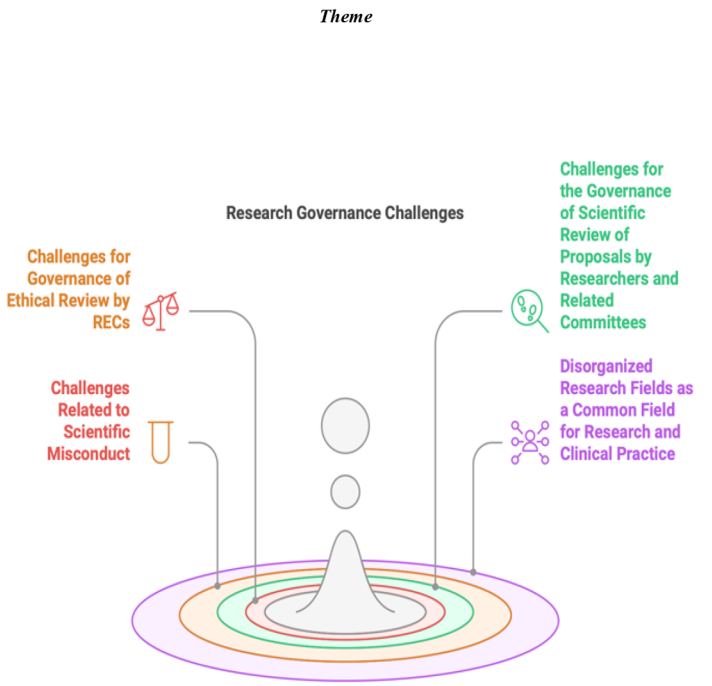
ID	Years of experience	Field of study	Highest Level of education	COVID-19 Research Activity (Researcher and Principal Investigator)	Providing Clinical Care to COVID-19 patients (Attending Physician, Nurse,)	Membership in RECs	Research administration and governance experience During COVID-19 Pandemic
1	25	Biomedical ethics	PhD	-	-	*	*
2	15	Biomedical ethics	PhD	-	-	*	*
3	26	Biomedical ethics	PhD	-	-	*	*
4	20	Biomedical ethics	PhD	*	-	*	*
5	13	Biomedical ethics	PhD	*	-	*	*
6	18	Epidemiologist	PhD	*	-	*	*
7	19	Pediatrician	MD	*	*	-	-
8	22	Pharmacist	MD	*	-	*	*
9	25	Pharmacist	MD	*	-	*	*
10	10	Neurologist	MD	*	-	-	*
11	22	Infectious disease specialist	MD	*	*	*	-
12	18	Infectious disease specialist	MD	*	*	*	-
13	11	Gastroenterologist	MD	*	*	-	-
14	14	Biomedical ethics	PhD	*	-	*	*
15	16	Nurse	MS	-	*	-	-
16	3	Internist	MD	*	*	-	-
17	6	Internist	MD	*	*	-	-
18	7	Infectious disease specialist	MD	*	*	-	-
19	15	Nurse	MS	*	* COVID-19 ICU Head Nurse	-	-
20	20	Immunologist	PhD	*	-	*	-
21	20	Nurse	PhD	*	-	*	-
22	13	Epidemiologist	PhD	*	-	*	*
23	8	Nurse	MS	*	*	-	-
24	7	Nurse	MS	*	*	-	-
25	20	General Physician	MD	*	*	-	*
26	12	Internist	MD	*	*	-	-
27	18	Pulmonologist	MD	*	*	-	*
28	30	Pulmonologist	MD	*	*	-	-
29	20	Medical Record Administrators	PhD	*	-	-	-
30	19	Biomedical ethics	PhD	*	-	*	*

technology" (no.6). There was also a feeling that international research projects involving Iran were unfairly labeled. As one participant noted, "Unfortunately, some official health authorities said that Iranians shouldn't be the Guinea Pig of foreign pharmaceutical companies, and this issue put pressure on RECs. It was an unfair labeling of participation in international research and possibly depriving the Iranian society of possible benefits" (no.2). Additionally, the repetitive nature and small sample sizes of some studies led to a lack of confidence in the findings, as one respondent mentioned: "Many small research projects were proposed with a small sample size, which were also repetitive, and because of the small sample size, there was no confidence in the findings" (no.11). Concerns about the approval of ineffective drugs were also raised, with one researcher stating, "One of my problems was that some ineffective drugs were approved, and I was worried" (no.4). The issue of pharmaceutical companies inducing a need for certain drugs was also noted: "Some opportunists also created an induced need for some drugs that were used in the research" (no.6).

Autonomy and the participants' right to self-determination

There were significant concerns about the informed consent process, with several participants noting that proper information was not always provided to participants due to time constraints or urgency. One researcher remarked, "Sometimes it was so urgent that there was no time at all, and we did not explain well. We just told them to fill out the form" (no.13). Another participant mentioned, "I think sometimes, unfortunately, we had to give little information to the patient and the family" (no.10). In some instances, patients were unaware that blood samples were being taken for research purposes, as expressed by a participant: "Many times, we took blood from the

Table 3 Theme 1, substantive ethical values & principles



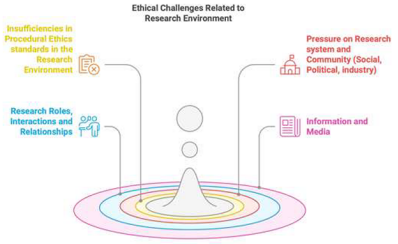
Category	*Subcategory*
Challenges for Governance of Ethical Review by RECs	Pressure on RECs for Fast Approval and expedited and facilitated review
	Lack of enough human and financial resources for RECs
	Challenges for review of international proposals with participation
	Receiving proposals that lack of acceptable scientific justification or with major scientific and methodological problems
	Inconsistent ethical review process of proposals between different RECs
	Evaluation of competency and researchers for conducting research
	Low quality of ethics review by some RECs
	Lack of enough experience of all RECs for ethical evaluation of all kind of research proposals
	Inefficient supervision of REC on the conduct of approved project
	Security-oriented environment for of conducting and publication of results
	Lack of required essential technical or regulatory infrastructures
Challenges for the Governance of Scientific Review of Proposals by Researchers and Related Committees	Lack of enough pre-clinical deliberation or fast move from theory to practice
	Scientific Competency of the Investigators
	Competency of Research Organization
	Weak Design and low quality of Research Proposals
Challenges Related to Scientific Misconduct	Starting before receiving approval or without applying for ethics approval
	Non-disclosure of adverse events to RECs
	Publication of false information
	Data falsification
	Failure to comply with authorship standards
	Unauthorized use of research data
	Insufficient declaring the competing interests
	Stigmatization of particular community!
	Financial deviations
	Deviation from the approved protocol
Disorganized Research Fields as a Common Field for Research and Clinical Practice	Participation of patients in multiple trials
	Using public health insurance resources for research projects

patient for the research work of some researcher or some doctor, while the patient did not know at all" (no.12).

Participants' and other People's well-being

A primary ethical concern was the difficulty in conducting risk-benefit assessments, particularly in the face of uncertainties. One researcher expressed the concern that patients could be harmed: "I always had the fear of harming the patient because I just assumed that a certain drug was beneficial, while there was no evidence for it" (no.23). The issue of access to essential drugs was also a significant concern, especially during the COVID-19 pandemic. A participant recounted the situation where social media pressure caused a shortage of the drug Favipiravir, noting, "In one case, one of the famous intensive care specialist physicians who had millions of followers on social media complained about the lack of access to one Favipiravir, which induced a lot of pressure on the health system and patients' families who tried to find the drug even on the black market" (no.2). In some cases, researchers approved off-label use of drugs in the absence of clinical evidence, which raised concerns about patient safety. One participant explained: "In some cases, researchers, including basic scientists, applied for ethics approval arguing that theoretically, off-label use of some products would be helpful for COVID-19. Because

Table 4 Theme 2, research environment

Theme	*Category*	*Subcategory*
	Pressure on Research system and Community (Social, Political, industry)	Research Hype among the Researchers
		Pressure from the pharmaceutical industry
		The direct intervention of non-academic political and military organizations in the research process
		Political support for Traditional Medicine
		Pressure of pseudoscience
	Insufficiencies in Procedural Ethics Standards in the Research Environment	Discrimination among researchers
		Lack of transparency in the allocation of research funds related to Covid-19
		Discrimination in the process of obtaining ethics approval
		Abuse and Exploitation of Clinical Staff and Medical Professionals for Research
		Inclusion and participation and engagement of the community
	Research Roles, Interactions and Relationships	Including of hospitalized patients in research studies and clinical trials without informing the treatment team and the attending physicians
		The lack of transparency in the research team's role
		Poor commitment of project partners
		Stressful and respectful clinical research environment
		Dual role of clinician-scientists as physician and researcher
	Information and media	Cyberbullying against researchers
		Premature press release of research results and rapid broadcasting of research results in media
		False claims by some researchers
		An emerging role of some social media channels on the research policymaking and process

no standard treatment was available for the disease, risk-benefit assessment was difficult. For example, some researchers claimed that Captopril [a drug that is normally used for blood hypertension] could help [COVID-19] patients because it is able to block the human cell membrane receptors [ACE2] that are used by the Virus to enter the cell" (no.2).

Justice and equity

There were concerns regarding fairness and equity in the distribution of resources and compensation. One issue raised was the unavailability of drugs for patients with the diseases that these drugs were originally intended to treat due to their off-label use in clinical trials. As one participant pointed out, "There was a risk of unavailability of certain products for patients with the disease that the drug was originally approved for, due to multiple clinical trials for off-label use of some drugs, such as those registered for AIDS and Hepatitis C" (no.2). Additionally, the equitable distribution of donated drugs from international organizations was also a point of contention, particularly as the system struggled to ensure that the most vulnerable populations had access to necessary treatments.

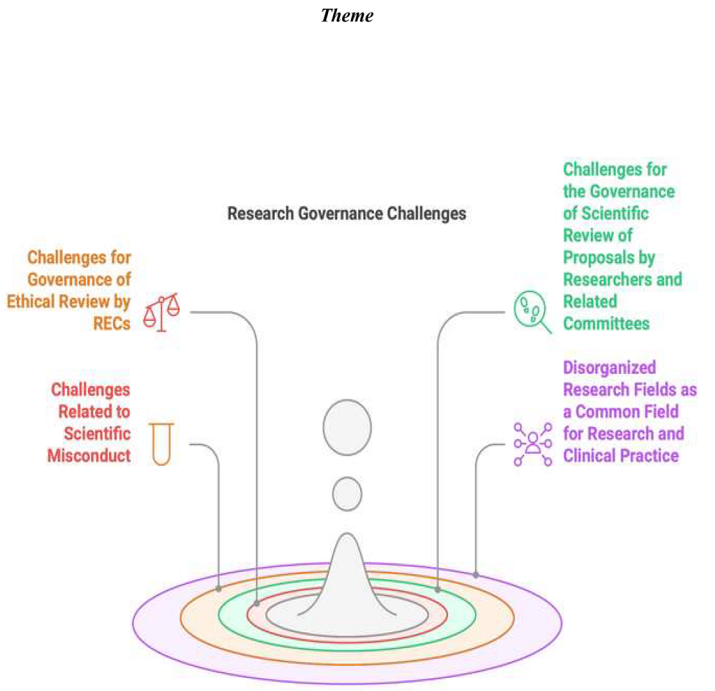
Research environment (Table 4)

The ethical issues surrounding research in the Iranian context can be classified into four main categories: Research Environment, Research Roles, Interactions, and Relationships, Information and Media, and Insufficiencies in Procedural Ethics Standards in the Research Environment.

Pressure on research system and community (social, political, industry)

The research environment in Iran faced significant external pressures, both from within the academic community and from non-academic actors. Researchers noted the prevalence of research hype, with individuals outside of academia—such as grocers and veterinarians—submitting research plans for approval, as one researcher stated: "Everyone had written a plan and sent it for approval. We had a pilot, grocer, and a veterinarian who had written a plan and wanted to try an intervention" (no.7). The political and military influence on research was also evident. A notable example was when a military commander introduced a virus detector, which was widely broadcasted on national TV, "There were cases of direct non-academic interventions by people in political and even military officials in the research or technologies related to the pandemic" (no.4). Moreover, pressure from individuals involved in pseudoscience, like homeopathy, was cited as another challenge: "A number of people who were active in pseudoscience such as Homeopathy and the like tried to influence the research system" (no.8). The ethical issues associated with these external pressures were compounded by the involvement of political figures, with one respondent commenting: "Meanwhile, the arrival of political and influential figures puts a lot of pressure on us to conduct research. They called from the office of

Table 5 Theme 3, research governance and management



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	Stigmatization of particular community!
	Financial deviations
	Deviation from the approved protocol
Disorganized Research Fields as a Common Field for Research and Clinical Practice	Participation of patients in multiple trials
	Using public health insurance resources for research projects

some powerful officials and said that this project must be approved" (no.9).

Research roles, interactions, and relationships

Ethical concerns also arose due to a lack of transparency and communication within research teams, particularly regarding the involvement of hospitalized patients in clinical trials without informing the attending physicians. One physician shared: "Sometimes the patient was involved in a study, but I, the attending physician, did not know at all. Or the study drug was not included in the patient's hospital chart" (no.9). There were also tensions between the roles of clinicians and researchers, with one participant stating: "The thing that put me under a lot of pressure was how far I should continue according to the research protocol. Or should I continue a drug to see if it is effective or not" (no.13). Another participant reflected on the difficulties of balancing the dual roles of clinician and researcher: "I could not create a balance between my roles as attending physician and researcher and it bothered me a lot" (no.19). These tensions were further exacerbated by interpersonal conflicts, as one individual noted: "It was a bad situation that sometimes the doctors treated each other with a bad word" (no.6).

Information and media

The role of information and media also raised significant ethical concerns. Some researchers were accused of prematurely releasing research findings to the media, sometimes making false claims about the efficacy of drugs before results were confirmed. One participant recalled: "Some colleagues and investigators of the projects interviewed the media, while the results of research had not yet been determined, sometimes they said that the drug was effective or that the treatment for had been discovered" (no.3). The media's impact was further amplified when a well-known intensive care specialist with millions of followers on social media complained about the lack of access to a drug, causing public pressure on the healthcare system: "One of the famous intensive care specialist physicians who had millions of followers on social media complained about lack of access to one Favipiravir, which induced a lot of pressure on the health system and patients' families who tried to find the drug even on the black market" (no.3). In some cases, social media outlets played a positive role in research oversight, with one respondent explaining: "During the pandemic, some channels of social media played a crucial role. They followed the news and reviewed the ethical approvals of research projects that in some cases helped the NCEBR to find some wrong and flawed approvals" (no.2).

Insufficiencies in procedural ethics standards in the research environment

There were also significant ethical challenges related to inefficiencies in procedural ethics standards. One issue was the discrimination faced by less powerful researchers, particularly younger academics. As one researcher explained: "When a person is well-known [powerful] in the system, all the staff of the organization are mobilized for him/her to do his/her work, while I, a young researcher, who just started my work and needs the same resources, I fall back completely" (no.3). In some cases, clinical staff were exploited for research purposes without proper recognition or compensation. One participant described the situation: "As a nurse, my work had really multiplied… Sometimes I did not even know what I was giving to the patient" (no.4). The lack of transparency in the allocation of research funds, especially related to COVID-19, further compounded these issues: "In the [COVID-19] pandemic the society was so sensitive about the research. It was the first time that the public had followed the research results on a daily basis. They were expecting the research community to do something. But there was no organized activity to engage the community with the research process" (no.5).

Research governance and management (Table 5)

Challenges for governance of ethical review by RECs

As it is mentioned by the study participants, one of the significant challenges faced by RECs during the COVID-19 pandemic, was the pressure for fast approval and expedited review processes, especially for international projects. For example, in the case of the WHO's Solidarity trial, local RECs, such as NCEBR in Iran, were waiting for WHO REC approval, but the lack of sufficient communication and official relations between the two bodies caused delays. As one respondent explained, "NCEBR was waiting for the WHO REC approval and WHO was waiting for local REC [In this case Iran NCEBR] to issue the final approval. The problem was insufficient communication and lack of official relation between WHO and NCEBR." (no.2). In addition to this, political and influential figures often exerted pressure on RECs to approve research projects. One respondent noted, "The arrival of political and influential figures puts a lot of pressure on us to conduct research. They called from the office of some powerful officials and said that this project must be approved." (no.9). Some RECs also approved projects that were ethically questionable, such as the approval of intravenous ethanol injection as a treatment for COVID-19. One respondent said, "Some RECs approved projects that were totally unacceptable, for example, the REC approved injection of Intra Venous Injection of Ethanol to humans as a treatment for COVID-19 disease." (no.2). other challenges included the submission of proposals by unrelated specialists, with one respondent mentioning: "Unrelated specialists also submitted research proposals for approval. For example, the people with administrative roles in hospitals and research institutions who based on their specialty had nothing to do with the proposed project." (no.9). Moreover, the intervention of security forces, especially concerning COVID-19 data, made some RECs hesitant to approve international or big-data projects, as described by a respondent: "Because of intervention of security forces specifically around the COVID-19 data, some RECs were hesitant to approve international or bid-data projects." (no.6). A lack of essential technical or regulatory infrastructure, such as GMP-grade facilities or appropriate biosafety levels for stem cell research, was another problem that RECs faced. As one respondent explained: "Sometimes our problem was that we did not know whether they had or could provide the equipment that were mentioned in the plan or not, such as GMP [Good Manufacturing Practice] grade clean rooms for Stem Cell Research or required Biosafety Level (BSL) for virus culture." (no.1).

Challenges for the governance of scientific review of proposals by researchers and related committees

In addition to governance challenges, there were significant issues related to the scientific review of research proposals. Some proposals lacked proper pre-clinical deliberation or rushed from theory to practice, which raised concerns about the quality of research. As one respondent pointed out: "Some proposals were submitted by a center where the center did not have the necessary expertise and resources to work." (no.8). Other issues included proposals that suffered from methodological flaws such as small sample sizes, insufficient samples, or vague information, with one respondent stating: "Some proposals suffered from obvious methodological problems. The sample size was small; or there were not enough samples to enter the study; or the work information was too vague." (no.5).Additionally, some research teams did not possess the required scientific competency, with one respondent noting: "A medicine that was apparently effective in research once became rare or was sold at a very high price." (no.2). Problems with weak design and low-quality research proposals were also noted, as well as a lack of sufficient experience in some RECs for ethical evaluation, which led to poor ethics reviews. One respondent commented: "Our work pressure was very high. We did not have a holiday. We were busy day and night evaluating plans and held gatherings one after another." (no.4).

Challenges related to scientific misconduct

Furthermore, there were cases where research teams started their work before obtaining ethics approval, violating basic ethical standards. As one respondent explained: "Some researchers started to work before obtaining the ethics approval." (no.2). Instances of scientific misconduct included deviations from the approved protocols, such as advertising for participant recruitment on social media without prior approval, with one respondent noting: "In one case, the research team deviated from the proposal and advertised to recruit participants on social media without receiving ethical approval for the public advertising, which could be a sensitive issue in a pandemic." (no.22). The ethical misconduct extended to financial deviations, such as researchers accepting money from patients in addition to funds provided by insurance and universities. One respondent described: "Unfortunately, some researchers took money from the patient, while the funds were paid both by the insurance and the university." (no.11).Additionally, the publication of false information, data falsification, and non-disclosure of adverse events to RECs were also serious issues. A respondent pointed out: "non-significant findings were not reported. Also, negative findings were not reported." (no.4).Another example of misconduct was the publication of a controversial paper that led to stigma in a local community. As described by one respondent: "In one case, the research team, deviated from the proposal and published their work without REC approval. The publication of the paper… resulted in some social objections and debates at the local level, which felt stigmatized because they thought that even if the prevalence of opium consumption is higher in this region, counting it as a cultural component is stigmatizing that community." (no.9).

Disorganized research fields as a common field for research and clinical practice

In the context of clinical practice, another challenge was the participation of patients in multiple trials, which often went unnoticed by attending physicians. One respondent explained: "Sometimes the patient was involved in a study, but I, the attending physician, did not know at all. Or the study drug was not included in the patient's hospital chart." (no.7). There was also concern over the use of public health insurance resources for research projects, with some projects drawing on resources that were intended for healthcare, which undermined the integrity of research and clinical practice.

Discussion

In this qualitative study, the ethical experiences of the participants related to COVID-19 research - in Iran were explained with three themes "substantive ethical values principles", "the Research Environment", and "Research Governance and Management".

Substantive ethical values principles

The theme "Substantive Ethical Values and Principles" refers to the following issues: lack of open discussion and clarification about the social value of international research conducted with the contribution of Iranian researchers and institutions; negative labeling of international research projects; approval of research studies with questionable social value due to expensive and hard-to-access interventions; challenges to autonomy and participants' right to self-determination.

The production of reproducible and generalizable knowledge, along with the improvement of society's health, are among the most important factors justifying the conduct of research. However, science must understand its role in society and be directed toward fulfilling this role. Limited research resources, particularly in LMICs, underscore the importance of prioritizing social interests when designing and conducting research. Consequently, the social value of research—defined as its potential benefit to society—is a fundamental ethical principle endorsed by international research ethics standards. RECs and other oversight bodies are expected to

uphold this principle, as conducting research without social value can adversely affect individual and public health while also wasting time, money, and human resources [21, 22]. In Iran, during the COVID-19 pandemic, various factors—primarily stemming from the unique nature of COVID-19 and its significant, visible impact on social and decision-making processes—brought the issue of social value in research design and implementation to the forefront. Determining an acceptable level of social value for research projects remains one of the most challenging aspects of ethical evaluation. This complexity was further heightened by the unprecedented volume of research projects and the significant uncertainty surrounding COVID-19 as a newly emerging disease.

One of the major shortcomings of research projects, particularly randomized controlled trials (RCTs), was the prevalence of small sample sizes and fragmented research efforts. Additionally, conducting repetitive studies without a synergistic direction posed a significant challenge, especially in the Iranian context. This issue was largely attributed to the high proportion of investigator-initiated research projects, which are typically funded through small grants from the internal budgets of universities. Meanwhile, well-resourced national granting bodies and wealthy pharmaceutical companies have minimal influence on steering the national research agenda.

However, since almost all medical universities in Iran operate publicly under the centralized governance of the Ministry of Health and Medical Education (MOHME), this body could have implemented more effective strategies for national-level research coordination. One specific instrument available for this purpose is a national portal for the synchronous indexing of all REC approvals. This portal enables research regulators, oversight bodies, and researchers to identify other research teams working on ethically approved projects in similar areas of interest by monitoring the publicly accessible indexed approvals.

Another issue raised by the participants in this study was the high cost of certain research interventions, such as projects testing advanced technologies like stem cell therapy or hemoperfusion. While, from a scientific perspective, there may have been valid justifications for exploring such hypotheses at the time of the studies, the unavailability of these interventions to the general public due to their high cost became a significant point of criticism. This criticism centered on the limited benefit and value of such research for Iranian society. Even if the results were promising, these interventions were often unaffordable for the public, and their widespread adoption could divert already scarce healthcare resources away from more essential medical interventions. This raises an ongoing question about the social value of conducting high-tech research in low- and middle-income settings, where resource constraints create constant competition between various healthcare priorities.

Many challenges related to the social value of research projects are associated with international studies conducted by institutions or companies from the Global North in LMICs. The COVID-19 pandemic was no exception. Due to Iran's relative marginalization in international research, stemming from financial sanctions imposed by the United States and its allies, internationally funded biomedical research projects are not commonly conducted in Iran. Despite these limitations, Iranian university hospitals played a prominent role in one of the global randomized controlled trials (RCTs) coordinated by the World Health Organization (WHO), known as the Solidarity Trial [23]. Notably, a significant portion of participants in the Phase 3 trial—designed to assess the efficacy of Remdesivir—were recruited by Iranian collaborators [24]. While this project was approved by the NCEBR, it faced considerable criticism due to the high participation of Iranian patients in the trial. This resistance to and hesitation about participating in international human studies can be better understood within the broader context of Iran's political interests and its government's distrust of Western powers. This sentiment was exemplified by Iran's Minister of Health during the COVID-19 pandemic, who publicly opposed the participation of Iranians in international COVID-19 vaccine clinical trials, asserting that Iranians should not be treated as "lab rats" or "guinea pigs" for foreign researchers [25, 26].

Obtaining informed consent from research participants is both a moral and legal requirement universally and in Iran. However, based on the experiences of participants in this study, this fundamental ethical principle of research involving human participants was not adequately respected during the pandemic. Evidence suggests that informed consent has been a persistent challenge in the Iranian research context even in non-pandemic situations [27–29]. The impaired practice of obtaining informed consent in clinical research during the pandemic, consistent with previous empirical findings, can be attributed to the paternalistic environment of clinical and clinical research practices in Iran [30–32]. This issue was further exacerbated by characteristics of the pandemic, such as the urgency to conduct research ("research rush") and the high level of scientific uncertainty, which made effective communication with patients more difficult. While earlier evidence highlighted issues with obtaining valid informed consent in clinical trials, the experiences of participants in this study revealed various forms of violations, including non-consent, deception in obtaining consent, and coercion of patients to participate in studies—a particularly severe breach [33, 34]. This alarming finding underscores the

potential of pandemic conditions to predispose research environments to blatant violations of participants' rights.

These observations highlight the urgent need for regulatory and oversight bodies to prioritize further research to assess the prevalence of such ethical breaches and develop strategies to address this critical challenge effectively.

Another significant challenge was the complexity and difficulty of conducting risk-benefit analyses for COVID-19 research projects. This was a predictable issue arising from the scientific uncertainties surrounding the novel and rapidly evolving nature of the disease [35]. While harming research participants is an unintended but sometimes inevitable consequence of human research studies, a more serious category of harm is misleading society about the results of such research.

This issue arose multiple times during the pandemic in Iran. For example, some researchers used public platforms and social media to prematurely claim therapeutic effects for certain interventions. In one notable case, a prominent university professor with millions of social media followers publicly criticized the lack of access to Favipiravir, claiming its therapeutic efficacy without robust scientific evidence. This claim exerted significant pressure on the healthcare system and patients' families, who sought the drug even on the black market. Authorities warned at the time that counterfeit drugs were being sold at exorbitant prices, leading to severe financial, psychological, and physical harm for patients and their families.

This case highlights that misinformation is not limited to laypeople or non-specialists. In the absence of clear education and sufficient guidelines, even scientists can become sources of misinformation, with potentially greater harmful consequences. Such actions not only risk undermining public trust in medical research and clinical practice but also exacerbate existing challenges.

Another example involved multiple clinical trials testing off-label uses of Hepatitis C and HIV antiviral drugs. These trials not only created risks of shortages for patients who required these drugs for their approved uses but were accompanied by media interviews where some principal investigators prematurely claimed the effectiveness of these drugs. This misinformation misled the public, adding to the confusion and distrust during an already challenging time.

Among other possible factors, such misrepresentation by the research community could be attributed to various intentions and reasons, including researchers' therapeutic misconceptions, potential conflicts of interest, a desire for heroism, or the pursuit of social attention. These factors had a significant impact on the country's response to the pandemic. Surprisingly, Remdesivir—despite not being recognized as a standard treatment at the time—was incorporated into the MOHME's national guidelines for treating COVID-19 patients. Consequently, substantial financial resources were redirected to pharmaceutical companies manufacturing Remdesivir. This issue is particularly critical given that Iran was, and continues to be, grappling with severe economic challenges, largely stemming from financial and economic sanctions imposed by the United States. While other factors, such as pressure from manufacturers, may have influenced the widespread use of Remdesivir, this aspect warrants careful evaluation. Notably, this drug was initially imported and registered in Iran for clinical trial studies.

Equitable use of donated drugs requires clear guidelines at the local level. To implement a transparent mechanism for this, the Vice-Minister for Research at the Ministry of Health and Medical Education (MOHME) officially proposed the establishment of a committee to monitor the equitable allocation of such resources [36]. However, there is no evidence that the proposed oversight body was ever established. Furthermore, organizations or entities sending medications that have not yet been established as standard treatments need to clarify their intentions and ensure their appropriate and equitable use and allocation in the destination country. For example, if these products are intended for clinical trials, they must be shipped according to the approved protocol. However, the pandemic situation made precise planning and predictions more challenging.

Research environment

The theme "Research Environment" focuses on the various pressures affecting the research process. These pressures arise from factors such as competition among researchers, the influence of the pharmaceutical industry, and the involvement of political, military, and non-academic organizations in research. Additionally, political support for traditional medicine, pseudoscience, and inadequate ethical standards complicate the research environment. Other challenges include discrimination among researchers, lack of transparency in the allocation of COVID-19 research funds, and the exploitation of clinical staff and medical professionals for research purposes. The commitment of research teams is also questioned due to weak engagement from project partners. Furthermore, challenges related to information and media, including cyber harassment and media bias, exacerbate the situation.

The COVID-19 pandemic created pressure to conduct research from various stakeholders, each with different intentions and expectations. On one hand, society expected the research community to act swiftly in addressing the emerging disease, which created stress for researchers [37]. On the other hand, researchers, driven by a sense of social responsibility, sought to respond to

these demands, often by emphasizing their findings [38]. In such situations, researchers may feel a moral obligation to counter non-scientific and pseudoscientific claims in the media, a common issue during crises. Additionally, the desire for quick publication may have contributed to the research "hype" [39]. In the Iranian context, this surge in research activity was significant. A simple search on the National Research Ethics Portal, which indexes all approved research project titles, reveals that, during the pandemic and continuing to the present, approximately 16,110 research projects were approved by Research RECs, including 1,077 clinical trials, based on data from the Iranian Registry of Clinical Trials [40, 41].

In Iran, the research surge was driven by several factors, one of which was the traditional medicine sector. Traditional medicine in Iran exists in two forms: folk practices and treatments provided by certain general practitioners. The Iranian bio political system generally supports traditional medicine as a non-Western alternative, reflected in the establishment of higher education programs and clinics within medical universities. However, this approach has faced significant criticism [42]. The COVID-19 pandemic provided advocates of traditional medicine with an opportunity to make bold claims, especially due to the lack of approved treatments.

The influence of this sector was evident across various levels of the research and regulatory processes, including RECs. Manufacturers, researchers, and others pressured different sectors of the research and approval process, including ethics committees and the Iran Food and Drug Organization (FDO), to grant approvals. In at least one instance, the FDO approved a product that had been officially investigated by the NCEBR, but the underlying data was deemed unacceptable. Similarly, pseudoscientific claims—such as detecting the COVID-19 virus using bio-resonance technologies or curing patients with so-called GANS water—sought ethics approval from RECs for their projects.

Not all ethical issues in research were related to participants; some respondents highlighted ethical concerns within the research system itself, which we categorize as procedural ethics shortcomings. One participant described the violation of justice and discrimination among researchers and institutions in accessing research resources. Issues included inequitable prioritization of research projects during the approval process, delays in starting research, unjust support throughout the research process, and unequal cooperation from health facilities and hospitals, all of which hindered achieving faster results. While prominent researchers played a crucial role during the COVID-19 pandemic, junior or less well-known researchers often felt marginalized. Although the pandemic worsened existing societal inequalities [43], and inequities were evident in the inclusion of diverse health participants [44], the principle of justice was less emphasized within the research community. This study identified the exploitation of medical staff and students as an ethical challenge, especially in research data collection. Nurses, students, and even attending physicians were often tasked with gathering data and monitoring outcomes during their shifts, without receiving any benefit in return. Medical students were sometimes forced to participate in data collection or even perform research interventions, sometimes unaware that their actions were part of a study. Even when they knew, they were unable to refuse involvement, often under the direction of senior attending physicians.

Abuse and exploitation of clinical staff for research were more common in university hospitals, where power imbalances between professors, senior physicians, and junior staff were more pronounced. In Iran's public healthcare system, which combines medical education, healthcare, and research under the Ministry of Health and Medical Education (MOHME), residents and medical students play a central role in providing public healthcare, particularly in tertiary and key public hospitals [45].

In clinical research, physicians often play a dual role as both caregivers and researchers. In Iran, national guidelines require that the principal investigator be a certified physician to ensure accountability and protect patient interests. The attending physician must either serve as the principal investigator or accept responsibility if another physician takes on this role. Research involving patients cannot proceed without the physician's knowledge or consent. However, the COVID-19 pandemic disrupted this model, with instances where physicians were not part of the research teams. This lack of interaction between clinicians and researchers became a significant ethical challenge, particularly due to the absence of clear guidelines for this new dynamic. Issues included clinicians being unaware of their patients' participation in studies, insufficient communication between clinicians and researchers, limited interaction between researchers and participants, and conflicting priorities between treatment and research teams. Additionally, the increased medical workload and the surge in research studies during the pandemic negatively affected the quality of research and further hindered collaboration between the two groups [46].

According to the participants in this study, the procedural values of transparency, accountability, and inclusion were not adequately upheld during the research process. Some members of the medical team were either not actively involved in the research, not well-informed about the project, or not officially recognized as part of the study team. Additionally, the relationship between the healthcare and research teams lacked transparency,

and there was confusion about accountability for both research and treatment responsibilities.

The role of media during the pandemic has been widely discussed. As COVID-19 spread, people were forced to stay at home, leading to increased use of the internet and cyberspace [2]. While many people relied on online sources for COVID-19 information, social media played a dual role in this process. The term "infodemic" refers to the rapid spread of both true and false information simultaneously. Social media significantly influenced the distribution of health information during the pandemic, but it also contributed to the spread of misinformation, both intentionally and unintentionally. In such an environment, assessing the accuracy of medical information becomes challenging, as vast amounts of information reach large numbers of people quickly. Despite some questionable data being published in peer-reviewed journals, the consequences of misinformation were severe [47, 48]. For example, during certain periods of the pandemic, alcohol poisoning-related mortality was estimated to be eight times higher than usual. However, less attention has been given to the intersection of media and research during the pandemic [49].

"An interesting phenomenon in Iran during the pandemic was the activity of individual science journalists who primarily used their personal pages or social media channels for disseminating information. In Iran, all RECs' ethical approvals are indexed in a publicly available portal. These individuals monitored this database for newly approved projects and clinical trials related to COVID-19. Notably, they flagged some problematic approvals that were later retracted by the NCEBR, and some RECs were suspended by the NCEBR. These individual activists unofficially assisted the NCEBR in implementing a monitoring mechanism for all ethical approvals."

One significant issue observed in the Iranian context was the premature broadcasting of research results and press releases in the media. This was largely due to the absence of clear guidelines, which could have led to harm to individuals and eroded public trust in the research community. In response to such press releases—often issued before peer-reviewed publications—the Iran NCEBR secretariat introduced an emergency regulation requiring researchers to refrain from discussing the success of treatments before receiving approval from the FDO [50]. However, more detailed and sophisticated guidelines are necessary to address the variety of news releases. These could differ across dimensions such as emergency vs. normal situations, pre- vs. post-regulatory approval, and the societal and patient impact of the claims, as well as whether the claims are made before or after peer-reviewed publication.

While various social, cultural, personal, and institutional factors may contribute to such behaviors, it is crucial for oversight and regulatory bodies to treat such acts as misconduct in order to protect public health. This should apply to both researchers and the media. While false claims in academic papers are often addressed seriously, leading to retraction and other consequences, false claims in the public domain have not received the same level of attention. It is also important to establish rapid mechanisms for detecting and responding to such claims. One possible strategy is to utilize existing entities, such as RECs, or establish new advisory bodies to review press releases before they are publicly announced.

Researchers' use of media to release public opinions extended beyond press releases. During the pandemic, many researchers became "research celebrities," sharing not only information about their work but also their views on various pandemic-related projects and issues. This raises important questions about the moral responsibility and legal accountability of these researchers, particularly when they are recognized as official academic staff at universities or research institutions. These issues should be further analyzed and addressed to ensure researchers are held accountable for their actions.

Based on participants' experiences, cyberbullying was a significant challenge for researchers. The easy access to digital platforms and increased familiarity with the online space facilitated this phenomenon. During a time of extensive research, some researchers were vulnerable to threats and insults across different platforms. While an informed audience can mitigate the severity of such insults, the stressful and uncertain environment of the COVID-19 pandemic diminished this protective effect. Aboujaoude and Savage note that cyberbullying exists in different cultures, affecting all age groups, particularly adults. Therefore, special legislation is needed to prevent and mitigate the consequences of cyberbullying in various societies and cultures [51].

Research governance and management

The theme of "Research Governance and Management" highlights various challenges in the ethical and scientific review processes, including issues related to scientific misconduct. These challenges involve pressures to speed up approval processes, limited resources, and inconsistencies in ethical review procedures. Researchers often submit proposals lacking sufficient scientific justification, which results in inconsistent evaluations and inadequate oversight.

The COVID-19 pandemic highlighted the essential role of RECs in evaluating and ensuring proper research conduct. However, several factors made the operation of RECs difficult: the sheer volume of studies, the hype surrounding research, poor-quality study protocols, limited technical and financial resources, lack of experience, challenges in maintaining REC independence, extreme

workloads, time constraints, poor coordination between researchers and ethics committees, and imbalanced committee compositions [38, 40, 41, 52].

The pandemic significantly impacted the research review process in several ways. Striking a balance between quality review and the rapid review required during public health emergencies is an ongoing challenge in all settings. This issue is particularly exacerbated in LMICs due to difficulties in accessing resources.

Another key challenge is the relationship between scientific and ethical reviews. In the Iranian context, Research Ethics Committees (RECs) only accept research proposals that have already been reviewed by a scientific review committee. While this provides more confidence for REC members, particularly regarding issues related to risk-benefit analysis, it can also lead to disagreements among stakeholders. For example, when REC members, some of whom are researchers or research methodologists, raise concerns about the scientific or methodological aspects of the study, conflicts may arise. In such cases, back-and-forth communication between the scientific review committee and the REC is often expected. Researchers sometimes argue that RECs should not question specific aspects of a proposal already reviewed and approved by the scientific committee. However, it is important to recognize that the REC members' understanding does not always align with this expectation. They rightly claim the right to raise issues related to the scientific aspects, as these are intrinsic to evaluating the social value of research, risk-benefit analysis, and the safety of participants. These challenges are intensified during public health emergencies, where the rush to conduct research can create additional pressure.

Another significant challenge was the inconsistency in REC approvals. In some instances, one REC approved a proposal, while another rejected it. This led investigators with rejected proposals to apply for ethics approval from different committees, which could cause further issues. For example, researchers could blame the REC that initially rejected the proposal. To address this, Iran's NCEBR modified the national portal for research ethics to allow REC administrators to view both rejected and approved proposals. This change helped RECs track the history of proposals and reduced multiple submissions of the same proposal to different committees after rejection. However, this situation underscores the importance of improving communication between RECs and enhancing vertical oversight mechanisms.

The high volume of research projects and time constraints increased the likelihood of mistakes or inadequate reviews. To address this, NCEBR implemented a post-approval surveillance policy in Iran. The national portal enabled synchronized monitoring of REC activities and reviews. As a result, many approvals were re-evaluated, several were retracted, and four RECs were suspended due to significant weaknesses, such as approving a proposal for intravenous injection of ethylene (alcohol). NCEBR used strategies like inviting experts in high-risk areas (e.g., traditional medicine and natural products) to support the post-approval surveillance system. This mechanism requires a legal framework to allow a central body, like NCEBR, to regulate other RECs.

During public health emergencies, there is an understandable expectation for expedited ethics reviews from researchers, society, health authorities, and political sectors [53, 54]. One study participant emphasized the importance of equity in prioritizing research for review. Clear guidelines, based on transparent and defensible criteria (e.g., study importance, order of application, study nature), could help RECs prioritize ethical reviews fairly. Additionally, screening and expedited review options should be considered for specific cases. In Iran, NCEBR issued a regulation requiring RECs to provide feedback to investigators within 48 h [50]. However, many RECs reported that poor scientific review and flawed study designs, such as low sample sizes, were their primary challenges. These challenges are interdependent, as difficulties in scientific review can also affect ethics review [43]. Another challenge faced by RECs was the lack of experience in evaluating all types of research proposals. One solution was to classify research types based on sensitivity and complexity, as Iran's NCEBR did for COVID-19 vaccine trials, which were reviewed solely by NCEBR. A further challenge involved assessing investigators' competencies, particularly when basic scientists proposed clinical trials.

Conclusion

The findings of this study explain participants' experiences of ethical challenges in COVID-19-related research in three areas. The study shows that the involved parties experience ethical challenges in various aspects related to both substantive and procedural issues. While most of these challenges exist even in the absence of a public health emergency such as a pandemic, the pandemic exacerbates the current challenges and makes the gaps more visible. The results emphasize that the process of ethics review in health research is part of a larger system that includes other pillars such as scientific review and regulatory bodies. It highlights the importance of all related sectors working in concert to create the necessary environment for preserving ethical values while conducting research during public health emergencies.

Addressing these challenges requires actions at different levels of health research policymaking and regulation, including international, national, and institutional levels, to prepare the groundwork and research environment for conducting ethically acceptable research. Therefore,

the development of clear guidelines and frameworks specifically designed for critical situations, such as pandemics, is essential. These frameworks must be adaptable to clinical research settings to maintain a balance between research goals and protecting individuals' rights. In the area of the research environment, societal and industrial pressures and the lack of clear ethical standards indicate the need to strengthen research ethics infrastructure and training at different levels of research and clinical practice. In the area of research management, problems such as inconsistencies in ethical and scientific review processes, scientific misconduct, and research and clinical interference indicate the need to establish more transparent and coordinated oversight systems. The development of unified and international standards for the ethical and scientific evaluation of research, along with the establishment of tools that facilitate review process and communication between various stakeholders and improve research ethics oversight, can help reduce these challenges. These results not only pave the way for reforming ethical policies in research and clinical practice, but can also be used as a guide for managing similar challenges in future crises. Adopting a multidisciplinary and interdisciplinary approach can help better integrate ethical principles into practice and research and have long-term positive impacts on the scientific community and health systems. Research ethics training for researchers and clinicians and the development of protocols for better coordination between research teams are critical requirements.

Limitations

One limitation of this study was that the participants were mainly from Tehran, the capital. However, since some were members of the NCEBR and other national committees at the Ministry of Health and Medical Education, their perspectives could reflect the situation across the country. In addition, ethical challenges may be influenced by specific cultural, social, and political contexts. Some participants may shape their responses based on social or personal expectations, which can affect the authenticity of the data.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12910-025-01193-6.

Supplementary Material 1

Acknowledgements
The researchers would like to thank all the participating.

Author contributions
Contributors SM and ESH-G conceptualized the paper. SM conducted the interviews, and SM, ESH-G, and AP analyzed the data. All authors interpreted the data. SM and ESH-G drafted the paper. All authors critically revised the manuscript for important intellectual content.

Funding
The study was conducted with the financial fund of Digestive Diseases Research Institute under grant numbered 50485-97-3-99 At the Tehran University of Medical Sciences.

Data availability
The information obtained from the findings is presented in the table and in the article. Also, the typed interviews of the participants and the initial tables resulting from the analysis of the interviews and the initial codes are available in Persian.

Declarations

Ethics approval and consent to participate
This study was conducted in accordance with the Declaration of Helsinki and was approved by the Research Ethics Committee of Digestive Disease Research Institute at Tehran University of Medical Sciences, approval number: IR.TUMS.DDRI.REC.1399.041. The study information including aims and methods was explained and clarified for participants and their Informed consent for participation was obtained before the start of interviews.

Language editing and mind maps
The manuscript is now subjected to thorough language editing utilizing professional editing services provided by (Springer's editorial service) as well as AI-based tools (ChatGPT Version 1.2025.014 (1737150122)) to ensure linguistic accuracy and clarity. The resulting text after utilization of professional service and AI tools was carefully read and edited by authors to ensure accuracy of edits and fidelity of the original purpose of authors in the text. The mind map figures are designed by Napkin-ai.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 3 October 2024 / Accepted: 6 March 2025
Published online: 17 March 2025

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