

COVID-19 effect on clinical research: Single-site risk management experience

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Abstract

Background: The ongoing coronavirus disease 2019 (COVID-19) pandemic is extensively impacting new and ongoing clinical trials of various medical products irrespective of indication. It has the potential to adverse effect not only in terms of recruitment and immediate patient care but is also likely to affect the data collection and analysis in the months to come.

Aim: The aim was to illustrate the effect of COVID-19 on the clinical research in one of the research centers in low limited-resource country as Egypt and the management plan performed to decrease this adverse impact.

Methodology: Secondary data were collected anonymously about the measures implemented to deal with the challenges of conducting the nine ongoing and new clinical researches during COVID-19 pandemic at Faculty of Medicine, Ain Shams University Research Institute-Clinical Research Center.

Results: Out of the 47 enrolled participants, thirty participants required investigational product (IP) dispensation during the remaining study period; 27 of them had their IP dispensed at site, and six participants who were from far away Governorate were not able to come to the center due to the partial lockdown and had their IP deliver through courier to their home. Safety laboratory assessment had performed at the site or local laboratory at their hometown. Virtual visit alternatives to in-person visits for communication and patient evaluation had been performed. Recruitment of new participants and opening new sites were stopped in many trials. In order to reduce the on-site activities, in particular, on-site monitoring, all monitoring visits were performed virtually.

Conclusion: The adverse impact of COVID-19 pandemic on clinical trials could be lessening by active management plan.

Keywords: Clinical research, clinical trials, coronavirus, coronavirus disease 2019

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INTRODUCTION

As of early 2020, humanity is confronting a pandemic with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that causes coronavirus disease 2019 (COVID-19).^[1] Since its

detection in December 2019 in China,^[2] it is still spreading in multiple countries and has already affected several million people.^[1] During March 1–28, 2020, the overall laboratory-confirmed COVID-19-associated hospitalization rate in the United States was 4.6/100,000 populations.^[3]

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Preventive measures such as social distancing, respiratory hygiene, frequent handwashing, and wearing face coverings in public settings were recommended by the Centers for Disease Control and Prevention (CDC).^[4] CDC recommends that travelers avoid all nonessential travels to the following destinations: China, Iran, Most European Countries, the United Kingdom, and Ireland. The CDC recommends that travelers avoid all nonessential travels to all the global destinations.^[5] Quarantine as a preventive measure is used to keep someone who might have been exposed to COVID-19 away from others.^[6]

Among many challenges thrown up by the pandemic, managing clinical trials where either trial participants or personnel or both may become unavailable for in-person visits is one. Furthermore, research centers that conduct the trials may no longer be easily accessible or safe to trial participants. In addition, there may be difficulties with the supply chain, as well as the availability and access to the products being investigated. As the situation continues to evolve, extraordinary measures may be required to be implemented to deal with these challenges and in ensuring the rights, safety, and well-being of participants while preserving the integrity of the trial conduct itself. The article describes the impact of COVID-19 on the clinical research in a research center in Egypt and the measures rolled out to mitigate the impact.

METHODOLOGY

Study design

Secondary data were collected anonymously about measures implemented to deal with the challenges of conducting both ongoing and new clinical research during COVID-19 pandemic between January 1, 2020 and April 22, 2020. Data were anonymized to maintain privacy and confidentiality.

Site of study

The Faculty of Medicine, Ain Shams University Research Institute-Clinical Research Center (MASRI-CRC) is well centered inside Ain Shams University Hospitals and is dedicated to carry out clinical research (human participants) and is committed to improve health outcomes and to enhance and expand the magnitude of high-quality clinical research (<https://masri-eg.com>). MASRI-CRC is integrated with harmony and collaboration with all departments and hospitals that include around 350 intensive care unit beds, 2000 inpatient beds, 70 surgical rooms, 33 endoscopies, and 140 outpatients' clinics and with catchment of around 1,500,000 inpatient/year and 500,000 outpatient/year.

Data collection

One researcher was responsible for extracting the data for this study from the MASRI-CRC database including registration database, follow-up report, and ethics committee communication (with special emphasis on initiating new trials and recruiting new participants as well as measures implemented by the local ethics committee during pandemic).

Data collection also included measures implemented to deal with the challenges of conducting nine ongoing clinical trials with 47 participants in the face of the pandemic.

Statistical analysis

Analysis of data was done using the Statistical Program for the Social Sciences version 17 (SPSS Inc., Chicago, IL, USA). A descriptive statistic was used to summarize and quantitatively describe the features from the collected information.

RESULTS

Measures implemented to deal with the challenges of conducting nine ongoing clinical trials with 47 enrolled participants are discussed in the following sections:

Investigational product

1. Investigational product (IP) availability at site: All IPs available at the site were reviewed, and all IPs required were ordered as far in advance as possible through couriers.
2. IP dispensation to participants: Out of the 47 enrolled participants, thirty participants required IP dispensation during the remaining study period, as illustrated in Figure 1.
 - i. Twenty-seven participants who were from Cairo and nearby Governorates had their IP dispensed at their scheduled visit at sites, and the participants returned their unused/used medications of the previous visit for accountability and assessment of compliance
 - ii. Six participants were from faraway Governorate and were not able to come to the center due to the partial lockdown that was implemented nationally between 7 PM and 6 AM. The new dispense IP was delivered through contracted courier to their home following the designed pathway: first, the site staff communicated with participants to confirm their inability to travel to the site. Second, the sponsor informed and gave their approval for arrangement to IP shipment through courier, and local European Commission (EC) informed through e-mail, and confirmation of EC approval

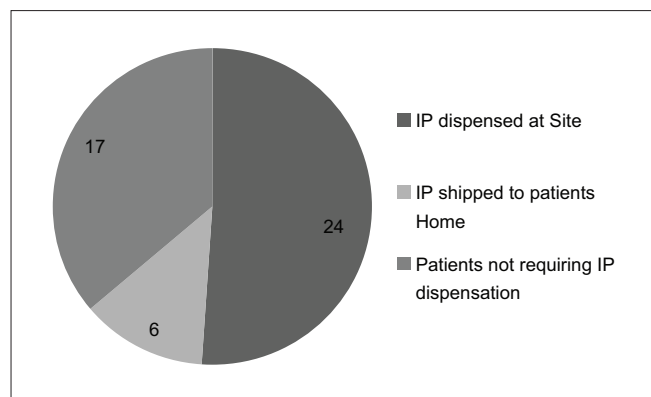


Figure 1: Investigational product dispensation procedures during the coronavirus disease 2019 pandemic

was obtained. Then, the courier representative received the new dispensed IP and shipped IP under controlled regulation maintained IP in permissible temperature. Finally, participants received IP allocated to him/her, instructed not to start taken it except after site staff reviewed the data logger reading to confirm that the medication is suitable to be used. Site staff followed up with the participants the instructions and ensured that they received their medication as per the protocol.

Laboratory assessment

Shipment of patient samples

Egypt has stopped passenger flights coming in and going out of the country. Three trials involved shipping of sample; site staffs contact the courier to determine if patient samples can be shipped before any scheduled patient visit. One trial had contracted a courier company; this company implements contingency plans and was able to ship samples. The second trial the site staff could not ship the sample; these samples were collected as per the protocol and stored till the time of the site able to ship the samples and ensuring that the storage condition is well monitored to preserve the samples. The third trial, unfortunately, the laboratory kits were expired, and consequently, no samples were withdrawn from the enrolled participants.

Laboratory kits availability

The stock of laboratory kits was reviewed and staff determined if sufficient stock within the expiry date for any upcoming participants' visits was available or not. If it was sufficient, the staff orders all laboratory kits required as far in advance as possible. The kits' importation takes a longer time, and more regulation is needed. In one of the trials, the kits were expired and importation was delayed, the required samples were not collected and protocol deviation was filled, and the sponsor was informed.

Safety laboratory assessment

The safety laboratory had been performed for all enrolled participants as per the protocol at the site. Tele-consultation was performed with all the participants to confirm their ability to make the visit and to search for a laboratory that could perform the assessment, and five participants confirm their inability to come to the site. Four participants out of those five have a branch of an assigned, accredited, contracted Egyptian laboratory located at their hometown, and consequently, laboratory assessment was performed as per the protocol. One patient who did not have any branch for the assigned laboratory performed his/her assessment at the nearest local laboratory at his hometown. None of the participants received the IP except after ensuring that the safety laboratory result is received.

Patient care

On-site visits were performed whenever possible and if not feasible, then virtual visits as alternatives were implemented for participants' evaluation:

1. Reporting adverse events and concomitant medication changes were performed through telephone visit with patient/caregiver and then documented in participants' source documents and recorded in the electronic case report form (eCRF)
2. The acceptability of the formulation (palatability) was assessed as per protocol for one of the ongoing trials through on-site visit for two participants and through video call for another five participants
3. Questionnaires as pediatric quality of life inventory sickle cell disease (SCD) module and fatigue total score were completed as per protocol for one of the ongoing trials through on-site visit for two participants and through phone call for another five participants. Phone call was then documented in the source documents
4. Clinical examination including vital data and anthropometric assessment were performed on the on-site visit, where both participants and site staff were wearing mask and follow the hand hygiene precaution for 27 enrolled participants with certain arrangement for 13 of them, who were from far away area to be transported by private car that include only the patient and caregivers to decrease any exposure, as illustrated in Figure 2. Virtual training was performed for a physician working at the nearest governmental hospital about what is needed, and a broad training about good clinical practice was given. The trained physician then performed the assessment for the five participants who could not come to the site
5. Visit required special procedure as electrocardiography (ECG) was performed as per protocol on the on-site visit except for the five participants from faraway

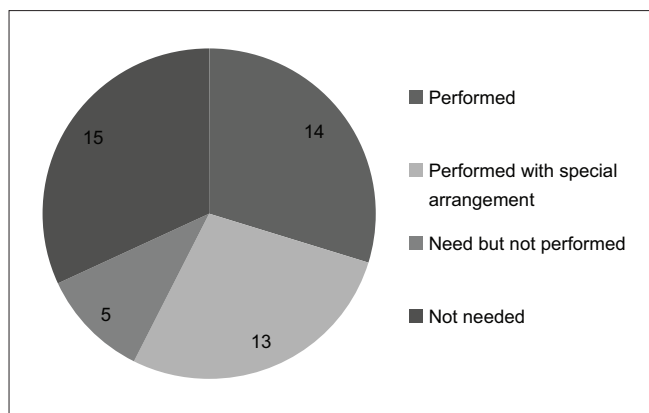


Figure 2: On-site visit during the coronavirus disease 2019 pandemic

Governorate who had their ECG performed at a local hospital at their hometown

6. Trial participants were contacted regularly to confirm that none were infected with the virus.

Starting a new clinical trial or recruiting new trial participants in an ongoing trial

These activities were going on at the start of the pandemic in January, February, and the first half of March and then the recruitment was suspended based on sponsor decision.

Virtual European Commission meetings

Virtual EC meetings were performed and were allowed communication and approval through soft copies sent through e-mails.

Sponsor challenges

In order to reduce the on-site activities, in particular, on-site monitoring, all monitoring visits were performed virtually after getting the approval of EC.

DISCUSSION

The center was conscious about the consequences the COVID-19 pandemic had on the conduct of clinical trials; the present work illustrates single Egyptian clinical research center experience during the current pandemic to decrease the adverse impact of COVID-19 pandemic on the clinical research. This experience may provide some advice regarding conducting clinical trials in countries in our region. The center implemented measures that are intended to preserve the activities of the trial as far as possible while protecting the participants' safety and well-being. Ensuring that participants had enough IP supply was one of the top, and IP was dispensed to all participants and delivered through courier to their home whenever need. Safety laboratory assessment were performed to ensure the safety profile while participants were still on the study. Virtual visits should be considered as an alternative to

in-person visits for communication and patient evaluation. Recruitment of new participants and opening new sites may be wise to be suspended. In order to reduce the on-site activities, in particular, on-site monitoring, all monitoring visits were performed virtually.

Globally, the CoVID-19 pandemic alerts the international scientific bodies to the need to implement extraordinary procedures to regulate and control clinical trial during the pandemic. These measures should include the informed consent process, in-site study visits and procedures, data collection and data recording on eCRF, study monitoring, adverse event and changes in concomitant medication reporting, and changes in investigator(s), site staff, and/or monitor(s) secondary to travel restrictions, quarantine measures, or COVID-19 illness itself.

Following the first detection of SARS-CoV-2 in Wuhan,^[7] several organizations acknowledge the impact of COVID-19 on the health system and broader society, and the impact it may have on clinical trials and trial participants including the European Medicines Agency, Good Clinical Practice Inspectors Working Group, the Clinical Trials Facilitation and Coordination Group (a working group of the Heads of Medicines Agency), the Clinical Trials Expert Group (a working group of the European Commission representing Ethics Committees and National Competent Authorities), and the EC.^[8] The Food and Drug Administration (FDA) published a new guidance for industries, investigators, and institutional review boards that is aimed at ensuring the safety of trial participants as well as the integrity of clinical trials during the Covid-19 pandemic. The FDA acknowledges the need for amendment of clinical trial protocols due to this evolving health crisis and stated that changes will depend on the particulars of each trial including participant population, location, and medical products used.^[9]

All the bodies work in the field of the clinical trial including sponsors, investigators, and ECs should consider establishing and implementing policy and procedures to describe approaches to be used to protect trial participants and manage study conduct during possible disruption of the study as a result of COVID-19 control measures at study sites. These policy and procedures should be compliant with applicable (regional or national) policy for the management and control of COVID-19.^[10] These measures should be designed to feasible to be implanted in any global concern in an attempt not to delay the scientific research and maintain the right and safety of participants.

CONCLUSION

The COVID-19 pandemic continues to have a greater

impact on the operations of research institutions and their clinical development activities. This effect could be lessening by active management plan.

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Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Casadevall A, Pirofski LA. The convalescent sera option for containing COVID-19. *J Clin Invest* 2020;130:1545-8.
2. Garg S, Kim L, Whitaker M, O'Halloran A, Cummings C, Holstein R, *et al.* Hospitalization rates and characteristics of participants hospitalized with laboratory-confirmed coronavirus disease 2019 — COVID-NET, 14 States. *Morbidity Mortality Weekly Rep* 2020;69:458-64.
3. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, *et al.* Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020;382:1708-20.
4. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/diy-cloth-face-coverings.html>. [Last accessed on 2020 Apr 26].
5. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/travelers/map-and-travel-notices.html>. [Last accessed on 2020 Apr 26].
6. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/social-distancing.html>. [Last accessed on 2020 Apr 26].
7. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, *et al.* Clinical features of participants infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:497-506.
8. Available from: https://ec.europa.eu/health/sites/health/files/files/eudralex/vol10/guidanceclinicaltrials_covid19_en.pdf. [Last accessed on 2020 Apr 26].
9. Available from: <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-issues-guidance-conducting-clinical-trials>. [Last accessed on 2020 Apr 26].
10. Novara D. Coronavirus Pandemic (COVID-19) Clinical trials advice. *Clin Res Trials* 2020;6:1-2.