International Journal of Clinical Trials
Kalra D et al. Int J Clin Trials. 2020 Nov;7(4):235-244
http://www.ijclinicaltrials.com
pISSN 2349-3240 | eISSN 2349-3259
DOI: https://dx.doi.org/10.18203/2349-3259.ijct20204480

Original Research Article

Challenges faced by investigators in conduct of oncology trials during COVID-19 pandemic at Tata Memorial Centre: a cross-sectional survey

Devanshi Kalra[1], Abhidnya Desai[2], Amit Joshi[3], Gouri Pantvaidya[4]*

[1]Clinical Research Secretariat, [2]Institutional Review Board, [3]Medical Oncology, [4]Surgical Oncology, Tata Memorial Hospital and Homi Bhabha National Institute, Mumbai, Maharashtra, India

Received: 10 September 2020
Accepted: 08 October 2020

***Correspondence:**
Dr. Gouri Pantvaidya,
E-mail: docgouri@gmail.com

ABSTRACT

Background: Novel corona virus disease 2019 (COVID-19) pandemic has impacted health care sector adversely and its major impact is seen especially in the field of oncology. One of the areas of cancer care that has been affected is the conduct of clinical trials. Various challenges have emerged in front of the investigators in providing proper treatment and care to the research participants and moreover in safeguarding the rights, safety and well-being of the research participants.
Methods: A questionnaire survey was conducted among the oncologists from the major specialties (medical, surgical and radiation) during the lockdown period to assess the challenges faced in conduct of clinical trials during this pandemic.
Results: A total of 110 questionnaires were circulated. Of the 110 questionnaires distributed at the Tata Memorial Centre, 50 responded. The overall response rate was 45.45% (50 responses). Majority of investigators (96%) reported that the pandemic affected the initiation of new trials in oncology. 86% investigators reported that COVID-19 situation has resulted in more protocol deviations than usual for ongoing trials also 62% investigators expressed that the quality of the trial data may get affected due to pandemic.
Conclusion: Our survey reports that the majority of the researchers are encountering major challenges in conducting clinical trials in an oncology setting during this pandemic. Despite these challenges in trial conduct, efforts are being made by the investigators and their team to adapt to the new methods for effective management of patients in clinical trials.

Keywords: COVID-19, Pandemic, Clinical trial, Oncology

INTRODUCTION

On March 11th 2020, the World Health Organization (WHO) declared the novel Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) outbreak a pandemic.[1] Its impact is majorly seen on the Health care delivery, severely affecting the patients care.

Individuals with cancer, particularly those who are receiving systemic anticancer treatments, have been postulated to be at increased risk of mortality from COVID-19.[2]

Two studies published in The Lancet indicate a high rate of mortality among COVID-19 patients who also have cancer. In a study conducted in US, researchers analyzed data on more than 900 COVID-19 and cancer patients from the United States, Canada, and Spain and found that 13% died. In the other study, it was found that, in an analysis of 800 UK patients with COVID-19 and cancer, 28% of the patients died.[3]

One of the areas in the cancer care that has been especially disrupted by COVID-19 is the conduct of clinical trials. The disease has the potential to impact the scientific

integrity and patient safety of the ongoing trials, increased operational burdens on the trial programs, and has limited access to trials and newer therapies for all patients. Trial programs may be unable to meet all of the protocol-specific requirements and procedures, such as protocol-mandated tumour biopsies, outpatient visits, laboratory/diagnostic testing including imaging, and completion of patient questionnaires. This may lead to protocol modifications and/or deviations (intentional or unintentional) with unknown consequences.[4]

Irrespective of how much longer the pandemic lasts, clinical trials will remain disrupted for several months. Data integrity of ongoing trials is likely to face additional evaluation- specially to find out whether the results were influenced by the ongoing COVID-19 pandemic.[5]

Various measures are being taken by various sponsors and regulatory authorities to help in dealing with the current situation taking into account the rights, safety and well-being of the trial participants. Regulatory authorities like CDSCO, DCGI (India), FDA and National Institutes of Health (USA) and MHRA (UK) have released various suggestions and guidelines on how to deal with clinical trials during the ongoing COVID-19 pandemic. CDSCO has allowed sponsors to reconsider, suspend, or terminate ongoing trials. Drug regulator understand the challenges faced by clinical trials in the background of the massive COVID-19 pandemic.[5]

Taking into consideration the above factors, we decided to conduct a survey in our setting to identify the problems faced by investigators in conduct of various clinical trials during the pandemic.

METHODS

A questionnaire was designed taking into account various possible problems faced by the investigators during this pandemic in the oncology setting, that were addressed in various articles published during this period. Also help was taken from the Institutional Ethics committee looking at the nature of deviations and violations received during this time period, on various clinical trials. The study was conducted for a period of 02 months from May to June 2020.

Development of questionnaire

A comprehensive search of published literature on conduct of oncology clinical trials during COVID-19 was performed using PubMed and Google Scholar. Oncology clinical trials, pandemic and COVID-19 were used as keywords in various combinations. A list of relevant articles was identified along with relevant cross references.[1] Literature was reviewed, and an exhaustive preliminary list of relevant questions was prepared. This was then discussed amongst the co- investigators who were specialists from the fields of medical and surgical oncology to give a balanced multidisciplinary coverage and applicability across all specialties of oncology. The questions were then finalized with the broad aim in mind i.e. to incorporate relevant challenges in conduct of clinical trials during the COVID-19 pandemic.

The final questionnaire (Appendix 1) was formulated in two parts. Part 1 consisted of a profile of respondents and their experience in oncology while part 2 consisted of questions pertaining to challenges faced in conducting trials during the ongoing pandemic.

Institutional ethics committee approval was sought and registration was done on Clinical trial registry of India (CTRI/2020/05/025218).

Survey methodology

The questionnaire was circulated among the oncologists of Tata Memorial Centre. The survey was initiated via an online portal (main website: https://docs.google.com/forms).

All non-respondents received reminders at a period of two weeks to ensure better response rates. Questionnaire was served maintaining strict anonymity of the investigators.

Statistical analysis

Data were maintained and analysed in Statistical package for the social studies (SPSS) version 25 (IBM SPSS Statistics, Armonk, NY: IBM Corp). A descriptive analysis was performed.

RESULTS

A total of 110 questionnaires were circulated. Of the 110 questionnaires distributed at the Tata Memorial Centre, 50 oncologists responded. The overall response rate was 45.45% (50 responses).

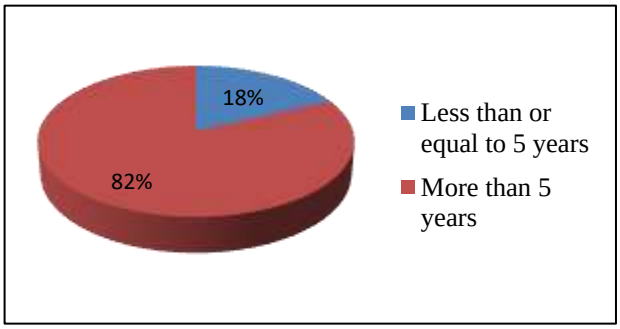

Figure 1: Working experience in oncology.

Responses

Part-1

A total of 82% (41/50) investigators had experience in oncology for more than 5 years where as 18% (9/50) of the

investigators had experience in oncology for less than 5 years.

Also, 26% (13/50) investigators were involved in conduct of investigator- initiated trials and pharma- sponsored trials.

Nearly 66% (33/50) of the investigators have been involved in national and international multicentric trials.

Table 1: Effect of pandemic, on patient enrolment in clinical trial.

Effect on patient enrollment			
Questions	**Responses**		
	Yes (%)	**No (%)**	**Not applicable (%)**
Effect on initiation of new trials in oncology	48 (96)	2 (4)	0
Ongoing trials had stopped accrual	30 (60)	15 (30)	25 (50)
Patients have shown hesitation to participate in the clinical trials	21 (42)	8 (16)	21 (42)

Part-2

Effect on patient enrolment

Around 96% (48/50) investigators reported that the pandemic affected initiation of new trials in oncology (both investigator initiated and pharma- sponsored trials). 60% (30/50) of the investigators, reported that their ongoing trials had stopped accrual due to the pandemic.

Also, 42% (21/50) investigators reported that patients have shown hesitation to participate in the clinical trials.

Effect in conduct of clinical trial

Around 60% (30/50) investigators reported that there was delay in trial related investigations due to the current situation. 78% (39/50) reported that trial participants are not able to visit the hospital on their scheduled visits.

Twenty eight percent (14/50) and seventy two per cent investigators reported that the pandemic has adversely affected the interactions between the study site and the sponsor and study site and the patient respectively.

All remaining observations with regard to effect of the pandemic on conduct of clinical trials have been elaborated in Table 2.

Table 2: Effect of pandemic, in conducting a clinical trial.

Effect in conduct of a clinical trial			
Questions	**Responses**		
	Yes (%)	**No (%)**	**Not applicable (%)**
Delay in investigations due to pandemic	30 (50)	8 (16)	12 (24)
Participants visit the hospital on scheduled visits	2 (4)	39 (78)	9 (18)
Interaction between the study site and sponsor	14 (28)	10 (20)	26 (54)
Interaction between the study site and patient	36 (72)	8 (16)	6 (12)
Trial participants enrolled on clinical trials continued to receive the required care	32 (64)	8 (16)	10 (20)
Patients' visit to the hospital has been affected	46 (92)	0	4(8)
Patient's treatment is being delayed	14 (28)	32 (64)	4 (8)
Follow up visits of trial participants are also affected	19 (38)	23 (46)	8 (16)
Logistic delay faced in procuring the investigational drugs from sponsor	7 (14)	6 (12)	37 (74)
Drugs administration is done as per protocol for active patients	18 (36)	6 (12)	26 (52)
Delay or interruption in investigational product/ study intervention	26 (52)	7 (14)	17 (34)
Investigators were able to contact the patients using other means of communication without patient's presence at site	30 (50)	9 (18)	11 (22)
Issues faced related to trial documentation due to shortage of staff	28 (56)	16 (32)	6 (12)
Time spent on patient counselling is affected	28 (56)	11 (22)	11 (22)
Problems faced in reimbursing patient's expenses	18 (36)	9 (18)	23 (46)

Effect of pandemic, on patient's safety assessment and data quality

Nearly, 54% (27/50) investigators reported that they were able to perform safety assessment for ongoing patients.

As per 60% (30/50) investigators were able to report Serious adverse event (SAEs) to the Ethics committee/Data safety monitoring unit/ Central licensing authority.

According to 86% (43/50) investigators, COVID-19 situation has resulted in more protocol deviations than usual for ongoing trials and 62% (31/50) investigators reported that the quality of the trial data may be affected due to pandemic.

Other results

Sixty two percent (31/50) investigators reported they are aware about the guidance issued by Central drugs standard control organisation (CDSCO) related to COVID-19 pandemic.

Nearly, 72% (36/50) reported that they have observed the pandemic affecting other oncology groups, sponsors, and/or cooperative groups.

Around 70% (35/50) investigators reported that there was lack of adequate resources for patients' management, physicians' safety and research protocol implementation.

DISCUSSION

The main focus of our survey was to highlight the challenges faced in conduct of oncology clinical trials during the COVID-19 pandemic.

Our survey highlighted some of the major issues like delay in initiation of new oncology trials and patients' uncertainty about their participation in the trials. It is observed that initiation of new trials was impacted due to limited access to resources and manpower constraints with reference to all the lockdown restrictions.

Majority of the investigators expressed that trial participants were not able to reach the hospital on their scheduled visits that has affected the enrolment rates and timely follow ups of the participants. Also, the patient safety was a major concern for the investigators due to lack of medical oversight.

Most investigators felt that the quality of the trial data will be affected due to the pandemic in view of increased number of protocol deviations. The deviations related to study assessments and investigations may affect the data integrity and study outcomes.

A few other surveys have also been conducted such as, ASCO (American society of clinical oncology) conducted a survey on early impact of COVID-19 on performance of oncology clinical trials. The survey highlighted various aspects relating to the research program policies and priorities, challenges in conducting clinical trial and relating to the opportunities to improve clinical trials. Major findings of the survey included that 64% of the respondents reported that their institutions had developed and instituted formal policies related to the COVID-19 pandemic, more than half of patients (54.8%) reported a decrease in patient ability or willingness to come to the site and the time required by the staff to organize, implement, and conduct telehealth visits was a significant challenge.[6]

Upadhaya et al also conducted a survey on impact of COVID-19 on oncology clinical trials. The survey indicated that patient enrolment in active oncology trials was negatively affected at the time of the pandemic especially in US and Europe where as it did not have much impact on Asia at the time survey was conducted. In the published study, 60% of investigators reported that the COVID-19 pandemic had 'moderate' or 'high' impact on patient visits (delayed or cancelled). The majority (~80%) of the respondents anticipated that protocol deviations would cause unresolved queries, such as incomplete patient visit data.[7]

Also, a survey was conducted by Parikh et al on the impact of COVID-19 on clinical trials in India. The major findings of the survey were stoppage of screening (55%), recruitment (62.5%), problems with adherence to study schedule (87.5%) and administration of study medication (42.5%) in clinical trials.[8]

In our survey it was reported that access to investigational drugs was not a major problem, as our hospital has a well-equipped research pharmacy. Investigational product (IP) management SOPs ensures adequate stocks of investigational products. Therefore, 36% of the investigators reported that beside the present situation, the drugs were being administered to the patients as per the protocol.

Majority of investigators indicated unavailability of adequate resources was a major hindrance to cope up with the pandemic situation. The limitation of our survey was that it included a small cohort of investigators who were involved in conduct of relatively heterogeneous types of trials (prospective or retrospective studies that may be investigator- initiated or pharma- sponsored). However, nearly 66% of the investigators who responded had experience in conducting national and international studies.

Considering coping strategies in the field of clinical research during this COVID-19 pandemic, one of the positive finding of our survey was that even during this period of escalating stress to cure the patients, the investigators and study team were keen enough to adapt to the new working environment such as tele-consultation services to communicate to the patients about the study

interventions/ other essential details relating to the trial. Also, there was no breach in reporting of safety data to the Ethics committee as large proportion of investigators could file SAEs and meet the reporting timelines during this pandemic, as TMH IEC has online submission portal, which proved to an advantage in this situation.

This survey will help us better understand the challenges faced in the field of clinical research while coping up with the pandemic. Adaptations to clinical trial practices during the pandemic are critical in ensuring patient access to both ongoing and new study treatments. In future, we expect more inclination towards the technological advancement such as telemedicine/real time consultation etc.

It is need of an hour to find solutions that could help in mitigating the effect of COVID-19 on clinical research and provide a long-term opportunity to improve and transform the clinical trial system.

CONCLUSION

COVID-19 pandemic has impacted the health care system globally. Consequently, its impact is seen clearly on the oncology clinical trials. Our survey highlights the aspects of oncology research that are affected due to pandemic with focus on the challenges faced by the researchers during this period.

The survey identifies and classifies these challenges encountered by the researchers in the execution of the clinical trials in the wake of pandemic. The institutions should develop working solutions and to adapt newer technological advancements for ensuring smooth conduct of clinical trials during emergency situations. Despite of the challenges, efforts are being taken up by the investigators to adapt to newer methods so that rights, safety and well-being of the trial participants are protected.

ACKNOWLEDGEMENTS

We thank all the investigators of Tata Memorial Centre for participating in the survey, thereby making this work possible to be shared in the oncology community.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Indini A, Aschele C, Cavanna L, Mario C, Bruno D, Giammaria F et al. Reorganisation of medical oncology departments during the novel coronavirus disease-19 pandemic: a nationwide Italian survey. Eur J Cancer. 2020;132:17-23.
2. Lee LYW, Cazier JB, Starkey T, Turnbull CD, Kerr R, Middleton G. COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study. Lancet. 2020;395(10241):1919-26.
3. Studies highlight COVID-19 impact on cancer patients. CIDRAP. https://www.cidrap.umn.edu/news-perspective/2020/05/studies-highlight-covid-19-impact-cancer-patients. Accessed June 25, 2020.
4. Waterhouse DM, Harvey RD, Hurley P, Levit LA, Kim ES, Klepin HD et al. Early Impact of COVID-19 on the Conduct of Oncology Clinical Trials and Long-Term Opportunities for Transformation: Findings From an American Society of Clinical Oncology Survey. JCO Oncol Pract. 2020:OP.20.00275.
5. CDSCO initiative to reduce impact of COVID-19 on clinical trials. https://www.m3india.in/contents/editor_pick/136066/cdsco-initiative-to-reduce-impact-of-the-covid-19. Accessed June 25, 2020.
6. ASCO Survey on Early Impact of COVID-19 on Performance of Oncology Clinical Trials - The ASCO Post. https://ascopost.com/issues/june-25-2020/asco-survey-on-early-impact-of-covid-19-on-performance-of-oncology-clinical-trials/. Accessed September 8, 2020.
7. Upadhaya S, Yu JX, Oliva C, Hooton M, Hodge J, Hubbard-Lucey VM. Impact of COVID-19 on oncology clinical trials. Nat Rev Drug Discov. 2020;19(6):376-7.
8. Parikh P, Mehta P, Kumar MVT K, Govind Babu K. Clinical trials facing "Serious Adverse Events" during the ongoing COVID-19 pandemic. Indian J Med Paediatr Oncol. 2020;41(3):295.

Cite this article as: Kalra D, Desai A, Joshi A, Pantvaidya G. Challenges faced by investigators in conduct of oncology trials during COVID-19 pandemic at Tata Memorial Centre: a cross-sectional survey. Int J Clin Trials 2020;7(4):235-44.

APPENDIX 1

Questionnaire

The conduct of the clinical trials that investigators are currently participating in may be impacted by COVID-19. This survey will help us understand the challenges faced by the Investigators during COVID-19 pandemic in the conduct of clinical trials at Tata Memorial Centre.

By filling and returning submitting this questionnaire, it is understood that you are consenting for the same. Your identity will be maintained anonymous. The data may be used for publication or research purpose.

Name of the Investigator:

Work Experience (in Oncology):

◯ Less than or equal to 5 years

◯ More than 5 years

Type of ongoing trials:

◯ Investigator- initiated

◯ Pharma-sponsored

◯ Academic- PG Thesis related

◯ All of the above

Type of studies:

◯ Multicentric International

◯ Multicentric within country

◯ Single Institution

Kindly fill this questionnaire and mark as appropriate. 1. Patients who have been enrolled and treated on clinical trials are still receiving the required care?

◯ YES

◯ NO

◯ NA

2. Is any of your active on going trial on hold presently, due to the pandemic?

◯ YES

◯ NO

◯ NA

3. Are you aware about the guidance issued by CDSCO (related to COVID-19 situation)?

◯ YES

◯ NO

◯ NA

4. Is the current situation affecting the patient's visit to the hospital?

◯ YES

◯ NO

◯ NA

5. Have patients shown hesitation to participate in trials recently?

◯ YES

◯ NO

◯ NA

6. Is there any compromise on investigations being performed as per the protocol due to current situation?

◯ YES

◯ NO

◯ NA

7. Are trial patients able to reach the hospital on their scheduled visits?

◯ YES

◯ NO

◯ NA

8. Are you facing any logistic delay in procuring the drugs from sponsor?

◯ YES

◯ NO

◯ NA

9. If yes (Q-8), please elaborate.

_____

10. Are you able to perform safety assessments for ongoing patients?

◯ YES

◯ NO

◯ NA

11. Are you able to follow drugs administration for active patients?

◯ YES

◯ NO

◯ NA

12. Is there a delay or interruption in any investigational drug/ study intervention based on the current situation?

◯ YES

◯ NO

◯ NA

13. Do you think the quality of the trial data, may be affected due to pandemic?

◯ YES

◯ NO

◯ NA

14. Do you think this pandemic will affect initiation of new trials in oncology (both investigator and sponsor initiated trials)

◯ YES

◯ NO

◯ NA

15. Has this pandemic, impacted the interactions between the study site and the patient?

◯ YES

◯ NO

◯ NA

16. Has this pandemic, impacted the interactions between the study site and the sponsor?

◯ YES

◯ NO

◯ NA

17. Do you think the COVID-19 situation may result in more protocol deviations than usual for ongoing trials?

◯ YES

◯ NO

◯ NA

18. Have you seen the pandemic affecting other oncology groups, sponsors, and/or cooperative groups?

◯ YES

◯ NO

◯ NA

19. Do you think patient's treatment is being done on time i.e. without any appreciable delay?

◯ YES

◯ NO

◯ NA

20. Are there adequate resources available for patients or physicians to overcome challenges during the pandemic?

◯ YES

◯ NO

◯ NA

21. Are proper follow ups being conducted for trial participants?

◯ YES

◯ NO

◯ NA

22. Are you facing any issues to notify any SAEs to the ethics committee/DSMU/ DCGI?

◯ YES

◯ NO

◯ NA

23. Is it convenient for you or your team to communicate to the patient about the study interentions/ other essential details relating to the trial using other means of communication (eg: telephone/ e-mail/ video interaction/ other means) without patient's presence at the site?

◯ YES

◯ NO

◯ NA

24. Are you encountering issues related to documentation/ transcription due to shortage of staff who are unable to attend regularly as before?

◯ YES

◯ NO

◯ NA

25. Has the current situation affected the time spent on patient counselling done by support staff?

◯ YES

◯ NO

◯ NA

26. Are you facing problems in reimbursing the patient expenses?

◯ YES

◯ NO

◯ NA

Please mention, any other challenge faced by you/your team in conducting trial in present situation (please specify):

Many thanks for your time and input!

Stay safe!