Original Article

Public disclosure of clinical trial results at Clinical Trial Registry of India- Need for transparency in research!

Renuka Munshi, Chaitali Pilliwar, Miteshkumar Rajaram Maurya

Department of Clinical Pharmacology, T. N. Medical College and BYL Nair Ch., Hospital, Mumbai, Maharashtra, India

Abstract

Introduction: Since June 15, 2009, clinical trial registration in the Clinical Trial Registry-India (CTRI) has been made mandatory by the Drugs Controller General of India to improve transparency, accountability, conform to accepted ethical standards and reporting of all relevant results of registered trials. In this study, we planned to evaluate the compliance of Indian and global sponsors with clinical trials conducted in India in terms of reporting of clinical trial results at the CTRI.

Methods: We included trials registered in the CTRI between January 2018 and January 2020. The CTRI and ClinicalTrials.gov registry was thoroughly searched for all completed interventional studies. A year-wise comparative analysis was performed to evaluate the number of clinical trials reporting results in both the registry.

Results: The reporting of completed interventional clinical trial results was 25/112 (22.32%) in year 2018, y, 8/105 (7.6%) in year 2019 and 17/140 (12.14%) in year 2020. There was significantly less reporting of results of Pharmaceutical company sponsored Interventional Studies-Indian at CTRI when compared with ClinicalTrials.gov registry for the year 2019 (odds ratio [OR]-0.17 (95% confidence interval [CI]: 0.08–0.36) and $P < 0.0001$) and year 2020 (OR-0.45 [95% CI: 0.24–0.82] and $P < 0.01$). The difference in results reported at CTRI was significantly low for Pharmaceutical company sponsored Interventional Studies-Global only for year 2019 (OR-0.09 [95% CI: 0.005–1.45] and $P = 0.04$) compared with ClinicalTrials.gov.

Conclusion: There is a need to develop the culture of reporting clinical trial results in CTRI to strengthen the transparency in the research for overall benefit of public, health care professionals, and research community.

Keywords: Central Drugs Standard Control Organization, clinical trials, interventional study, pharmaceutical, registry

Address for correspondence: Dr. Renuka Munshi, Department of Clinical Pharmacology, T. N. Medical College and BYL Nair Ch., Hospital, Mumbai Central, Mumbai - 400 008, Maharashtra, India.
E-mail: renuka.munshi@gmail.com
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INTRODUCTION

The Indian Council of Medical Research is a signatory of the WHO Joint Statement on Public Disclosure of Clinical Trials' results, adopted in May 2017. The signatories of this statement agree for the prospective registration and timely public disclosure of results from all clinical trials that is

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of critical scientific and ethical importance. The summary results of trials should be disclosed within 1 year of trial completion.[1-3] Scientific research and discovery are based on the principles of data sharing. It facilitates researchers to understand others' scientific work, identify any lacunae or limitation in the conduct of the study and work towards the improvement in study design for the advancement of science and community benefit. Dissemination of clinical trial results (whether negative, inconclusive, or positive) to the research community, the participants, and the public is a key aspect of conducting a clinical trial.[4,5] The impact of not sharing the results is detrimental. If the data remain unpublished, it leads to wastage of resources and time, as current and future researchers cannot benefit from the available information. There is reporting bias induced that can add to misinformation to the research and medical practice community. There are various ways to disseminate the study results of clinical trials such as by reporting the study results in the WHO clinical trial registry or in national registry.[5] The Clinical Trials Registry of India (CTRI) has developed a structured format for the disclosure of results for interventional clinical trials. CTRI promoted the registration of the clinical trials since it was launched in July 20, 2007 which was made mandatory from June 15, 2009 but the mandate for prospective registration of clinical trials was released on April 01, 2018.[6] The CTRI emphasizes the reporting of the clinical trials result after the study is completed. Individual patient data sharing or reporting is still voluntary.[7] The implementation of this into practice seems very far away. The advantages of reporting clinical trials result summary at the trial registry include the following: (1) help others to know and prevent the duplication of similar study conduct that may not add any scientific value, (2) saves time and resources in study conduct with no fruitful results, and (3) designing new clinical trials eliminating the methodological flaws and limitations.[8] At ClinicalTrials.gov registry of the US Food and Drug Administration (U.S. FDA), the clinical trial registration and results information submission requirements described in Section 801 of the Food and Drug Administration Amendments Act of 2007, known as FDAAA 801. The statutory requirements have been in effect since September 27, 2007, have been codified in section 402(j) of the Public Health Service Act, and include conforming amendments to the Federal Food, Drug, and Cosmetic (FD and C Act). The regulation became effective on January 18, 2017, and responsible parties have been required to be in compliance starting April 18, 2017.[9] There are several deficiencies narrated by Pillamarapu *et al*.'s study regarding the data entered into the CTRI such as lack of clarity in the classification of *Types of Studies*, internal inconsistencies, incomplete or non-standard information, missing data, variations in names or classification, and incomplete or incorrect details of ethics committees.[10] However, most of these deficiencies were addressed in the Letter to the Editor to the same journal by Maulik *et al*.[11] In this audit, we aimed to evaluate only the clinical trial results field of CTRI and looked for compliance of Indian and global sponsors with clinical trial site in India in terms of reporting of clinical trial results. We also wished to compare the proportion of studies that reported clinical trial results at CTRI with that of published data available at the US FDA Clinical Trial Registry called as Clinical Trials.gov maintained by the U. S. National Library of Medicine.[12]

METHODS

The study was exempted from ethics review as the data collected lies within the public domain. The CTRI was accessed at http://ctri. nic. in/Clinicaltrials/advancesearchmain.php on September 30, 2021, for data collection. The database was thoroughly searched using filters for all studies that have completed recruitment status and were interventional type of clinical trials. These also included filter set for primary sponsor as pharmaceutical studies-Indian as well as global with clinical trial site in India. Observational, BA/BE studies and post-marketing surveillance studies were excluded from the analysis. The 3 years' data of 2018, 2019, and 2020 were collected using appropriate keywords "CTRI/XXXX" where XXXX refers to year searched. For example, for the year 2020, the keyword used was CTRI/2020. At Clinical Trials.gov, an advanced search filter was used separately for country with and without India and searched for "Interventional studies" with completed study status and clinical trial results reported between first and last results updated dates of corresponding years. Finally, year-wise comparative analysis was performed with the proportion of Indian and global pharmaceutical sponsored completed interventional clinical studies that reported the clinical trial results data available from both CTRI and ClinicalTrials.gov registry to evaluate for any significant difference in terms of clinical trial results reporting.

RESULTS

Demographics

Number of studies with completed status-year wise

After performing the CTRI database search for only interventional studies, the number of studies with status updated as completed were 112 studies in year 2018, 105 studies in year 2019, and 140 studies in year 2020 [Figure 1]. The primary sponsor for these studies included both Indian

and Global Pharmaceutical sponsored companies. These numbers were used as denominators for performing further descriptive statistics for demographic data.

Number of studies reporting results at Clinical Trial Registry of India (ctri.nic.in)

The CTRI is working with WHO International Clinical Trials Registry Platform (ICTRP) to ensure that the results of all trials registered with the CTRI are adequately reported and publicly available. However, there are no specific timelines to report the results post-study completion. In the year 2018, only 25/112 (22.32%) interventional studies reported the results at CTRI. Similarly, 8/105 (7.6%) and 17/140 (12.14%) interventional studies results were only reported for the year 2019 and 2020, respectively. The difference in the number of reporting of clinical trial results across 3 years was statistically significant ($P = 0.006$).

Number of interventional studies with published data/ submitted to journals for publication

Of the total completed interventional studies in year 2018, 2019, 2020, only 4/112 [3.6%], 3/105 [2.8%] and 4/140 [2.8%] studies published their study with results or submitted their study data to the journals for the publication. There was no significant difference in the number of studies that were published or submitted their study data to journal for publication across three years [$P = 0.94$].

Number of studies that were regulated by the Central Drugs Standard Control Organization

There were 41/112 (36.6%), 36/105 (34.28%), and 42/140 (30%) studies with the Central Drugs Standard Control Organization (CDSCO) approved regulatory status in year 2018, 2019, and 2020, respectively. The rest of the studies were nonregulatory in nature and included the use of nutraceuticals, Ayurveda drug interventions or as postgraduate student dissertations which do not come under the direct purview of the Indian regulatory authority. Again the CDSCO-approved regulatory studies registered in CTRI database across 3 years made not much significant difference ($P = 0.53$).

Phase-wise distribution of completed pharmaceutical sponsored interventional studies

The number of interventional completed studies that were registered was maximum for phase 3 clinical trials followed by studies that were not categorized in any of these phases (NA) and phase 2 studies. Phase-wise distribution of the completed interventional studies is provided below [Figure 2].

Comparative analysis between Clinical Trial Registry of India versus Clinical Trials.gov

A comparative analysis was performed using the number of studies reporting clinical trial results in the CTRI versus the US FDA registry of Clinical trials.gov for each of 3 years 2018, 2019, and 2020. There was a significant difference in the reporting of clinical trial results between two trial registries for all Pharmaceutical-Indian studies in year 2019 and 2020 [Table 1]. There was a significant difference in the reporting of clinical trial results between two-trial registries for all Pharmaceutical company-sponsored-Global studies in the year 2019 [Table 2].

DISCUSSION

As per the National Regulatory Guidelines, clinical trials have to be registered in trial databases, before they are initiated and conducted. In the United States of America (USA), the National Institute of Healths (NIH), the National Library of Medicine maintains www. clincialtrials.gov, a database to register clinical studies, conducted in the USA or in any part of the world. Similarly, in India, it is mandatory that the clinical trials be registered in the Clinical Trials Registry-India (CTRI) before enrolment of study participants. The purpose of these databases is to

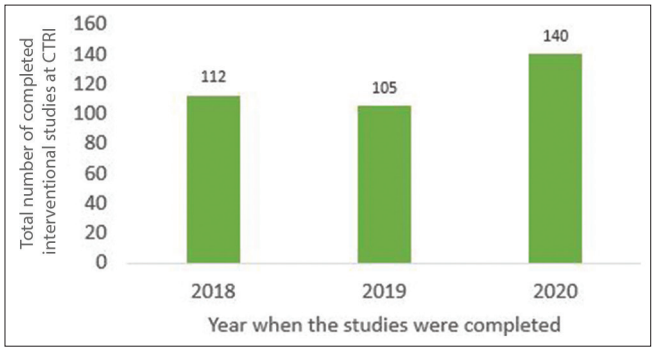

Figure 1: Number of interventional studies with completed status-year wise at CTRI

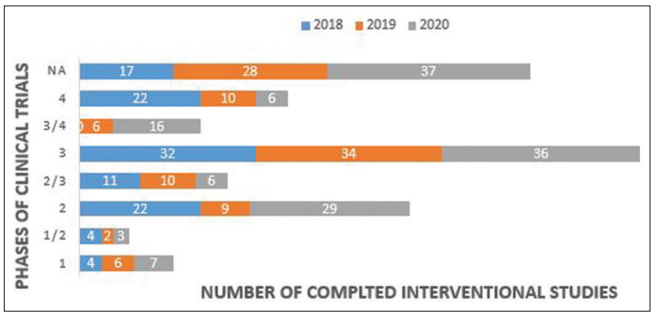

Figure 2: Phase wise distribution of the completed interventional studies at CTRI

Table 1: Clinical trials result reporting comparison for all pharmaceutical - Indian studies registered at Clinical Trial Registry of India and ClinicalTrials.gov

Clinical trial result reported at the trial registry (only pharmaceutical company sponsored - Indian studies)	Number of studies with results reported at CTRI, ICMR, Indian registry (%)	Number of studies with results reported at Clinical Trials.gov, US FDA based registry (%)	OR with 95% CI	*P*
Year 2018	19 (25.33)	98 (31.21)	0.75 (0.42–1.32)	0.39
Year 2019	8 (9.1)	123 (37.85)	0.17 (0.08–0.36)	<0.0001*
Year 2020	14 (13.08)	93 (25.2)	0.45 (0.24–0.82)	0.01*

*$P<0.05$ for statistical significance. Using 2×2 Chi-square statistics. CI=Confidence interval, CTRI=Clinical Trial Registry of India, FDA=Food and Drug Administration, ICMR=Indian Council of Medical Research, OR=Odds ratio

Table 2: Clinical trials result reporting comparison for all pharmaceutical - Global studies registered at Clinical Trial Registry of India and ClinicalTrials.gov

Clinical Trial result reported at the trial registry (only pharmaceutical company sponsored - Global studies)	Number of studies with results reported at CTRI, ICMR, Indian registry (%)	Number of studies with results reported at Clinical Trials.gov, US FDA based registry (%)	OR with 95% CI	*P*
Year 2018	6 (16.21)	5932 (24.03)	0.62 (0.25–1.46)	0.36
Year 2019	0 (0)	6934 (23.6)	0.09 (0.005–1.45)	0.04*
Year 2020	3 (10)	5691 (14.42)	0.71 (0.21–2.36)	0.77

*$P<0.05$ for statistical significance. Using 2×2 Chi-square statistics. CI=Confidence interval, CTRI=Clinical Trial Registry of India, FDA=Food and Drug Administration, ICMR=Indian Council of Medical Research, OR=Odds ratio

provide summary information of the studies, conducted in the respective countries, to the patients, their family members and the general public. The World Health Organization (WHO) maintains ICTRP and helps in conveying the relevant and complete information about the clinical trials including information related to clinical trial design, study conduct, and administrative aspects of the studies, to the general public. It will help those involved in healthcare decision-making to have up-to-date information on the clinical trial scenario across the globe. Apart from India and USA, there are many countries which maintain their own clinical trial registries including European Union, Japan, China, Korea, Australia, Brazil, Germany, Thailand, and Sri Lanka.[11] The present study was planned to analyze and evaluate the compliance of Indian and global sponsors with the Clinical Trials Registry-India (CTRI) in terms of reporting of clinical trial results and to compare the proportion of reporting of results with the US FDA Clinical Trial Registry called Clinical Trials. gov website. A total of 357 interventional clinical studies have been registered in CTRI from 2018 to 2020, as on September 30, 2021. The maximum number (39.2%) of clinical trials were found to be conducted in 2020 and this could be due to rise in research studies related to interventional therapy for COVID-19 that contributed 35.7% [50/140] of the total interventional studies (global and Indian pharmaceutical sponsored studies) registered at CTRI in the year 2020. Our study revealed that only few interventional completed studies, i.e., 14% out of the total (n = 50/357) reported results of their clinical trials on the CTRI website with statistically significant differences in the reporting across 3 years 2018, 2019, and 2020. India made the registration of clinical trials mandatory in 2009. However, reporting/submission of results and details of published results are only available for around a quarter of those registered till 2020, pointing to a lack of accountability and transparency.[13] Only 11 studies out of completed 357, i.e., 3.08% were published in a journal by the involved researchers with no significant difference across 3 years. In a previous study published in 2018, with an objective to evaluate the rates of publication for all completed randomized controlled trials registered in the CTRI database from July 2009 to December 2017, it was found that only 2.7% of studies mentioned the publication details (DOI, citation, ISSN) on the CTRI web portal.[14,15] This concludes that timely publication of Interventional regulatory studies sponsored by Pharmaceutical companies remains very poor even after recommendations and guidelines. Around 33.3% of clinical trials were regulated by CDSCO. A significant difference in the reporting of clinical trial results by Pharmaceutical company-sponsored Indian studies (interventional) was noted at ClinicalTrials.gov versus CTRI both in 2019 and 2020 which may be attributed to the stringent regulatory requirements of respective country. On the contrary, we see no reporting of clinical trial results at CTRI during the year 2019 and 2020, the year of COVID-19 pandemic outbreak with significantly more reporting on ClinicalTrials. gov (23.5%).[16]

CONCLUSION

The findings of the study suggest that despite mandatory registration of clinical trials and requirements to publish clinical trial results, this is not being adhered to by study sponsors as there is no strict government regulation or mandate to restrict trial activity for not reporting of the clinical trial results. The study concludes that Interventional

clinical trial sponsors need to report the study results in CTRI or provide publication details even if they publish the study results in medical journals or other databases so that this information is freely available to both general public and researchers in timely manner.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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