Overview of Ayurveda trials registered with Clinical Trial Registry-India: Need for customized data set items

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Abstract

Background: Lack of research data is one of the major challenges identified in traditional medicine (TM). Further, there is an urgent need to strengthen and streamline clinical research processes as well as develop research databases in TM. The Clinical Trials Registry-India (CTRI), a free, online primary register of the WHO’s International Clinical Trials Registry Platform, undertakes registration of all clinical trials being conducted in India, including TM trials. However, as the CTRI data set items are primarily designed to capture information of interventional trials of the conventional system of medicine, key fields relevant to the TM system are not adequately captured in the CTRI. Aims and Objectives: The current study was conceptualized with the objective to review the type and quality of trials registered in the CTRI as well as identify the specific data set items in CTRI which may be customized as per Ayurveda studies. Materials and methods: The trials registered from July 1, 2018, to March 31, 2020, were analyzed to decipher the kind of research being undertaken in the field of Ayurveda. These trials were manually reviewed independently by two Ayurveda reviewers to gain insights into the discrepancies. Along with these analysis, brainstorming sessions with Ayurveda experts were also held. Results: The fields which were identified and need tweaking and customization were the fields “health condition” and “intervention/comparator agent.” Conclusions: These modifications in the CTRI would enable the capture of more effective Ayurveda-specific information which would in turn help to standardize and streamline research practices as well as raise the standard of research.

Keywords: Ayurveda, Clinical Trials Registry-India, data set items

Introduction

Ayurveda is an ancient science of medicine, which is being practiced in India and neighboring countries for more than 4000 years. Its references can be found in Rigveda, one of the oldest extant texts. The word “Ayurveda” is composed of two Sanskrit words “Ayu” meaning life and “Veda” meaning science or knowledge; hence, Ayurveda is known as the “science of life.” Its holistic principles focus on personalized health with primary objectives being health promotion and disease prevention.[1] Even though Ayurveda is a well-documented science, in the era of evidence-based medicine, there is a call for its revalidation as per contemporary scientific requirements, i.e., clinical trials. Further, continuous research on the safety, quality and efficacy of Ayurvedic drugs and procedures and its documentation is needed to enable integration with the modern system of medicine. As per the WHO global traditional medicine (TM) survey report, 2012 and WHO global report on traditional and complementary medicine 2019, lack of research data was identified as one of the major challenges in TM. The report further stated that there was an urgent need to develop research databases in TM and strengthen research and evaluation of TM safety, quality, and efficacy.[2,3]

The Clinical Trials Registry-India (CTRI) is a free, online primary register of the WHO’s International Clinical Trials Registry Platform, for the prospective registration of all clinical trials being conducted in India, including trials of TMs such as Ayurveda, Yoga, Unani, Siddha, and Homeopathy (AYUSH).[4,5]
CTRI was launched on July 20, 2007, as a voluntary measure and since its inception, it has been hosted at ICMR-National Institute of Medical Statistics (ICMR-NIMS). The registration of clinical trials in CTRI was made mandatory by the Drug Controller General of India on June 15, 2009, which was further enforced by journal editors, ethics committees, and medical (including Ayurveda) colleges in the country.\[6\]

The CTRI collects key details of a clinical trial protocol, and once registered are freely accessible in the public domain. These data set items are largely applicable to clinical trials being conducted in modern medicine.

In this context, the Ayurveda trials registered between July 1, 2018, and March 31, 2020, were analyzed to decipher the kind of research being undertaken in this field and whether the CTRI dataset items needed to be tweaked to be able to faithfully capture Ayurveda specific data.

**Objective**

The objective of this article is to obtain insight into the characteristics of the Ayurveda trials registered in CTRI, analyze the obtained data and identify the CTRI dataset items that require customization according to the Ayurvedic system of medicine.

**Materials and Methods**

For this study, the data was extracted from the CTRI database (www.ctri.nic.in). All the interventional trials registered between July 1, 2018, and March 31, 2020, in which “Ayurveda” was cited as the “type of study,” were selected for analysis. CTRI has adopted to the International Classification of Diseases, Tenth Revision (ICD-10) for the health condition field, in June 2018, hence, trials registered from July 1, 2018, were taken for this study. The dataset items listed below were tabulated and collated on the basis of information provided by the registrant. The information collected for each of the registered trials included: type of trial; flagging of trials (prospective/retrospective); postgraduate (PG) thesis or others studies; type of primary sponsor (pharmaceutical industry/government funding/private medical college/others); gender and age of participants; phase of the trial (Phase I–IV); study design and randomization, number of centers (single center/multicenter), site of study and health condition of participants (healthy/patients) and intervention/comparator details (complete/incomplete).

In addition, these trials were manually reviewed independently by two Ayurveda reviewers and insights into the discrepancies were analyzed for correct, complete, and uniformity of information as provided by the registrant. Descriptive analyses were conducted on all characteristics of registered Ayurveda trials with a focus on the health condition. Assessment for intervention and details on total duration, frequency, mode of administration, and dose uploaded by the registrant was reviewed manually by the two reviewers. These parameters were scored based on health conditions and intervention details for completeness and appropriateness. Depending on the information provided, intervention/comparator details were classified as complete and incomplete.

Furthermore, in addition, an account of site/s of the registered trials were collated and analyzed vis-à-vis the consolidated list of Ayurveda colleges\[7\] for deciphering the regional trends of Ayurveda research in the country.

**Results**

Overall, 9721 trials were registered in CTRI from July 1, 2018, to March 31, 2020, and out of these, in 1392 “Ayurveda” was cited as the type of study.

**Descriptive analysis of the registered trials**

Table 1 gives the details of the registered Ayurveda trials. From the 1392 Ayurveda trials registered with CTRI, 1386 (99.6%) were interventional studies, 1349 (96.9%) were registered prospectively and 1068 (76.7%) were PG theses based studies.

Most of the trials, i.e., 1194 (85.8%), included participants of both sexes, 152 (10.9%) trials were on females only and in 46 (3.3%) trials were on males only.

As for the age of participants is concerned, 1166 (83.76%) trials included participants above 16 years of age (adults), 125 (8.98%) were conducted on children below 16 years of age and 101 (7.26%) included both adults and children as participants.
In 120 (8.6%) trials phase of the trial was mentioned as phase I, 175 (12.6%) were phase I/II trials, 299 (21.5%) were phase II, 190 (13.6%) were phase II/III studies, 130 (9.3%) were phase III, 35 (2.5%) were phase III/IV, 58 (4.2%) were phase IV and 18 (1.3%) were post-marketing surveillance studies.

Of the total 1392 trials, 23% were single-arm trials. Of the remaining 1065 multiple arms trials, 97% followed random allocation. Only 3% were in the nonrandomized category.

**Insights into the registered trials**

Analyses of these trials revealed that only 1353 were purely Ayurveda trials and 39 were multidisciplinary studies which included dental and other surgical and drug trials in combination with Ayurvedic drugs.

**Quality assessment of health condition**

Health condition which was coded as per ICD-10 codes, was analyzed [Table 2]. In about 60% of the trials, the correct ICD-10 health condition code was given and in the rest 40% of trials health condition was either incorrect, left blank, by mistake or due to the reason that the participants were healthy volunteers or it was a combination therapy (Ayurveda along with other system of medicine) trial. At present, there is no provision to accommodate this type of entry (healthy volunteers or combination therapy intervention) for Ayurveda trials.

**Quality assessment of intervention/comparator details**

Intervention and comparator agent names and details were analyzed in depth. Although 100% of trials provided the name of the intervention and comparator agent being used, however, information on details of Ayurvedic intervention, i.e., its dosage form, frequency, mode of administration and total duration of therapy was missing or incomplete in 511 out of 1392 (40%) trials.

**Assessment of the geographical distribution of Ayurveda trials**

Ayurveda colleges in the country were compared with the regional distribution of trial registration records in the CTRI [Table 3], and the table below clearly depicts the present situation with respect to the number of colleges vis-a-vis the number of trials registered during the specified period. The maximum number of trials are from Maharashtra followed by Karnataka, Gujarat, Rajasthan, and Delhi. Jharkhand, Goa, Haryana, Bihar, Punjab, and Uttar Pradesh were the states lowest in the tally and on an average conducted <1 Ayurveda trial in the period reported.

**Discussion**

The CTRI is a facilitator body that provides a platform for registering clinical trials prospectively, regardless of branch of medicine. In view of its utility in promoting transparency, accountability and accessibility of clinical trials, several organizations in the country such as the drug licensing authority, journal editors, ethics committees and
medical colleges, including Ayurveda colleges insist on trial registration.\(^\text{[7]}\) Dissemination activities undertaken by the CTRI yielded positive results and there has been a steady increase in the total number of trials registered over the years. Most trials were prospectively registered, single centric or academic trials conducted primarily on adults in government-funded institutions.

Overall Ayurveda trials accounted for more than one-seventh of the registered trials. Analysis of the dataset item “health condition” revealed discrepancies and inaccuracies and a need was felt regarding the inclusion of an Ayurveda-specific diseases categorization, which might have led to incorrect categorization by the registrant. Ministry of AYUSH had launched Namaste Portal (National AYUSH Morbidity and standardized terminologies Electronic Portal) on October 17, 2017. This portal provides information about standardized terminologies as well as morbidity codes for AYUSH health conditions.\(^\text{[8]}\) Thus, the Ayurveda health condition/morbidity codes from this portal are now integrated and implemented in CTRI for ease and uniformity for the researchers conducting trials in Ayurveda.\(^\text{[8]}\)

This analysis also suggested for need of modifications in the intervention/comparator agent section which are vastly different in principle and philosophy of practice in modern medicine vis-a-vis Ayurveda. Ayurveda has a unique way of disease management which includes Shodhana-Chikitsa (purification therapy), Shamana-Chikitsa (palliative therapy) and Shashtra-Chikitsa (surgery). Hence, along with drugs, procedures and lifestyle modifications including Dinacharya (daily regimen), Ritucharya (seasonal regimen), Sadvrutta (codes of conduct) are integral part of Ayurvedic management of diseases. In addition to this, drug dose, time of administration, duration of therapy and most importantly Anupana (co-administers with medicine) varies according to the condition and plays a crucial role in the treatment plan. Our analysis on quality of intervention details reflected that this section also needs to be customized to capture effectively, the complete information about the trial drug or procedure including its reference for dosage and/or duration. Pathya-Apathya which includes dietary and lifestyle

### Table 2: Quality assessment of health condition

| Error in health condition coding                          | Number of trials/total trials, \(n (\%)\) |
|----------------------------------------------------------|------------------------------------------|
| Correct coded                                            | 845/1392 (60.7)                          |
| Incorrect or blank ICD-10                                | 443/1392 (31.8)                          |
| Healthy volunteer                                        | 65/1392 (4.7)                            |
| Combination trials (Ayurveda + other system trials)     | 39/1392 (2.8)                            |

ICD-10: International classification of diseases, tenth revision

### Table 3: Region/state wise distribution of the registered trials

| State                        | Number of colleges (CCIM: 2016-17)\(^\text{[7]}\) | Total Ayurveda trials registered in CTRI | Average number of total trials conducted during the period |
|------------------------------|--------------------------------------------------|----------------------------------------|-----------------------------------------------------------|
| Andhra Pradesh               | 7                                                | 12                                     | 1.7                                                       |
| Assam                        | 1                                                | 7                                      | 7.0                                                       |
| Bihar                        | 8                                                | 2                                      | 0.3                                                       |
| Chhattisgarh                 | 5                                                | 9                                      | 1.8                                                       |
| Chandigarh                   | 1                                                | 1                                      | 1.0                                                       |
| Delhi                        | 2                                                | 104                                    | 52.0                                                      |
| Goa                          | 1                                                | 0                                      | 0.0                                                       |
| Gujarat                      | 20                                               | 260                                    | 13.0                                                      |
| Haryana                      | 11                                               | 2                                      | 0.2                                                       |
| Himachal Pradesh             | 3                                                | 9                                      | 3.0                                                       |
| Jammu and Kashmir            | 1                                                | 1                                      | 1.0                                                       |
| Jharkhand                    | 1                                                |                                        | 0.0                                                       |
| Karnataka                    | 67                                               | 294                                    | 4.4                                                       |
| Kerala                       | 18                                               | 69                                     | 3.8                                                       |
| Madhya Pradesh               | 19                                               | 19                                     | 1.0                                                       |
| Maharashtra                  | 71                                               | 385                                    | 5.4                                                       |
| Odisha                       | 6                                                | 7                                      | 1.2                                                       |
| Puducherry                   | 1                                                | 4                                      | 4.0                                                       |
| Punjab                       | 17                                               | 5                                      | 0.3                                                       |
| Rajasthan                    | 11                                               | 173                                    | 15.7                                                      |
| Tamil Nadu                   | 6                                                | 19                                     | 3.2                                                       |
| Telangana                    | 0                                                | 7                                      | .1                                                        |
| Uttarakhand                  | 10                                               | 63                                     | 6.3                                                       |
| Uttar Pradesh                | 48                                               | 30                                     | 0.6                                                       |
| West Bengal                  | 4                                                | 7                                      | 1.8                                                       |

CTRI: Clinical Trials Registry-India, CCIM: Central Council of Indian Medicine
Modification plays a very important role in Ayurveda treatment modalities. A separate section also needs to be added to capture the dietary and lifestyle modification-related interventions of the Ayurvedic system [Figures 1 and 2]. These modifications in the specific CTRI data set items would enable collecting more effective Ayurvedic system-specific pertinent information in the future and in turn, generating evidence, and help in raising the standard of research in Ayurveda. Brainstorming sessions with Ayurveda experts helped to customize this field as per Ayurveda requirements.

Most of the trials were conducted in Maharashtra (385), followed by Karnataka (294) and Gujarat (260). There were states such as Jharkhand, Goa, Haryana, Bihar, Punjab and Uttar Pradesh were the average number of trials conducted during the period reported are less than 1. This disparity in the average number of trials conducted underscores the urgent need for greater awareness regarding the crucial importance of the conduct of clinical trials and its registrations in the CTRI. The current analysis, identifying the discrepancies and gaps in the trials registered with CTRI, in the form of incorrect data such as the phase of trial, health condition as well as intervention and comparator agent details, indicates the need for spreading more awareness amongst the researchers from Ayurveda field through training/workshops on research methodology.

Conclusions
Clinical trials are considered the gold standard in the field of evidence-based medicine and CTRI offers the web-based platform where all the clinical trials including those being conducted in the field of Ayurveda are registered. The purpose of registration of all clinical trials is to improve transparency, accountability, and minimizing duplicate research and this can only be achieved if the information provided is uniform and complete. These newly developed customized datasets with the Ayurveda health condition codes as per the NAMASTE portal of the Ministry of Ayush and the modified intervention section, capturing all the Ayurveda system of medicine specific detailing, will assist in capturing quality data. With the concerted efforts of all stakeholders involved, this newly customized data set items in CTRI will help in strengthening, streamlining and standardizing the ongoing research in Ayurveda.

Launch of the Ayurveda dataset items on Clinical Trials Registry-India portal
The modified data set items, which were jointly developed by ICMR-NIMS and Central Council for Research in Ayurveda Sciences were formally inaugurated and launched on the CTRI portal by the then Honourable AYUSH Minister Mr. Kiran Rijiju on July 5, 2021. This is a significant step toward quality enhancement and acceptability of the research conducted in the field of the Indian System of Medicine, not only in India but worldwide.

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Conflicts of interest
There are no conflicts of interest.

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