Invited Article

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]

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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.

Figure 1: Launch of the Ayurveda dataset items on Clinical Trials Registry-India portal by the then Honourable AYUSH Minister Mr. Kiran Rijiju on July 5, 2021

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 and1068 (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.

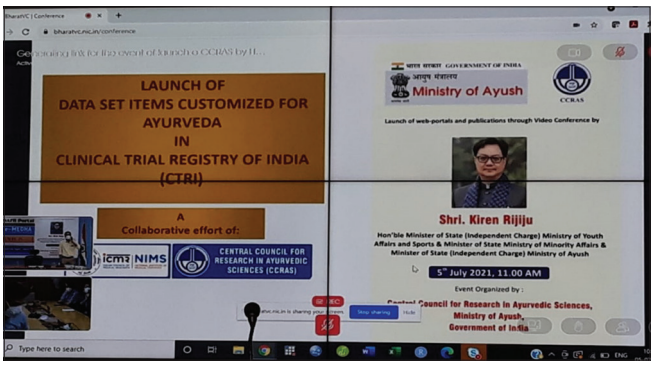

Figure 2: Launch of the Data Set Items Customized for Ayurveda

Tables 1: Characteristics of the registered trials

Description datasets	Number of registered trials, *n* (%)
Registration type	
Prospective	1349 (96.9)
Retrospective	43 (03.1)
Postgraduate thesis	
Yes	1068 (76.7)
No	322 (23.1)
Not specified	2 (0.2)
Primary sponsor	
Pharmaceutical industry	106 (7.6)
Government funding	625 (44.9)
Private medical colleges/hospital	261 (19.5)
Other	390 (28.0)
Gender	
Male participants	46 (03.3)
Females participants	152 (10.9)
Trials with male and female participant	1194 (85.8)
Age (years)	
Children (0-16)	125 (8.98)
Adults (16 and above)	1166 (83.76)
Both (0-99)	101 (7.26)
Phase of study	
Phase 1	120 (8.6)
Phase 1/Phase 2	175 (12.6)
Phase 2	299 (21.5)
Phase 2/Phase3	190 (13.6)
Phase 3	130 (9.3)
Phase 3/Phase 4	35 (2.5)
Phase 4	58 (4.2)
Others	385 (27.7)
Study design	
Single arm trial	327 (23.5)
Nonrandomized	
Nonrandomized, placebo controlled trial	3 (0.2)
Nonrandomized, active controlled trial	24 (1.7)
Nonrandomized, multiple arm trial	7 (0.4)
Randomized	
Randomized, parallel group trial	491 (35.3)
Randomized, parallel group, placebo controlled trial	86 (6.2)
Randomized, parallel group, active controlled trial	331 (23.8)
Randomized, parallel group, multiple arm trial	30 (2.2)
Randomized, crossover trial	8 (0.6)
Cluster randomized trial	6 (0.4)
Randomized factorial trial	4 (0.3)
Other	75 (5.4)
Health condition	
Patients	1314 (94.4)
Healthy human volunteers	78 (5.6)

A total of106 (7.6%) studies were sponsored by the pharmaceutical industry, 625 (44.9%) were government funded, 271 (19.5%) were funded by private medical colleges or hospitals and in 390 (28.0%) the primary sponsor type was stated as "others."

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.[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.[1] 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*.[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), *Sadvritta* (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)[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	.!
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 customizd 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[9] 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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