

An Audit of Clinical Studies Involving Elderly Population Registered in Clinical Trials Registry of India

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ABSTRACT

Context: The elderly in India form a heterogeneous subset of the population with significant disease burden variations. However, there are no data available regarding the type of research studies conducted in an elderly population in India. **Aims:** The aim of this study was to analyze the research studies conducted in the elderly population in India based on data from the Clinical Trials Registry of India (CTRI). **Settings and Design:** This was an “audit” of available data on the CTRI website. **Participants and Methods:** Following exemption from the Institutional Ethics Committee, all studies in the elderly population registered in CTRI from its inception (July 2007 to August 2019) were reviewed. Data captured with respect to geographical distribution, study designs used, therapy area, trial registration, and funding. **Statistical Analysis Used:** The variables were analyzed using descriptive statistics using SPSS version 16.0. **Results:** Out of a total of 21,400 studies in CTRI, a total of 99 (0.46%) studies involved only elderly patients. Of these studies, 60 (60.6%) were interventional, whereas 39 (39.4%) were observational. Of all the interventional studies, 17 (28%) tested drugs, 26 (43%) tested a lifestyle intervention, and the rest were nutraceuticals, Ayurveda, Yoga and Naturopathy, Unani, Siddha, and Homeopathy, and physiotherapy. Postgraduate theses constituted 60 (60.6%) studies. Eighty-seven (87.9%) were academic projects, eight (8.1%) were government-funded studies, and only four (4%) were pharmaceutical-sponsored studies. The most commonly studied therapy area was the central nervous system, followed by community medicine and orthopedics. **Conclusions:** This study depicts the underrepresentation of the geriatric population in clinical studies.

KEYWORDS: *Clinical Trials Registry of India, geriatric, vulnerable population*

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INTRODUCTION

People above 60 years of age are considered as “senior citizen” and constitute the “elderly” segment of the population in India.^[1] As per the 2011 census, the population of the elderly in India increased to 104 million compared with 57 million in 1991. There has been an increase in the proportion of elderly from 5.6% in 1961 to 8.6% in 2011.^[1] Currently, in a phase of demographic transition, the elderly population in India is projected to rise to 12% of the total population by the year 2025.^[2] The elderly in India form a heterogeneous subset of the population with significant variations in disease burden spanning across variables such as gender,

geographical location, socioeconomic status as well as diversity in culture and religion. They suffer from both communicable and noncommunicable diseases. An increase in communicable diseases is also observed as a result of decline in immunity as well as age-related physiologic changes.^[3]

The elderly contribute to patients’ significant burden for health conditions such as cancer, cardiovascular

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disease, arthritis, and Parkinson's disease, among others in most parts of the world. Furthermore, they form the majority being dependent on medications treating chronic conditions.^[4] There is inadequate evidence and knowledge about the responses of geriatric patients to medications. The older patient population is poorly represented in clinical trials, with up to 35% of published trials excluding older people. Poor representation of the elderly in clinical trials leads to inadequate evidence and knowledge regarding drug therapy in the elderly. Limiting older adults' participation by researchers may be due to their concerns about safety, risks of study procedures, and capacity to consent. Furthermore, the presence of comorbidities may confound treatment outcomes and lead to heterogeneity in treatment response.^[5] There were no data available regarding the type of research studies conducted in the elderly population in India.

Hence, the present study was designed to explore the type of clinical research conducted in the elderly population based on studies registered in the Clinical Trials Registry of India (CTRI).

PARTICIPANTS AND METHODS

The study was granted exemption from the Institutional Ethics Committee (EC/OA-109/2019). The audit included all the studies registered on CTRI from 2007 to August 2019. The Clinical Trial Registry website of India (www.ctri.nic.in) was searched using the keywords "elderly" and "geriatric" to identify all studies registered during the mentioned duration. Out of all the search results obtained, only those studies that included participants more than or equal to 60 years of age were only considered.

The variables assessed were the number of studies, the geographical distribution, types of study designs used (whether observational or interventional), the status of study whether ongoing or completed, therapy area, type of intervention tested, method of randomization, type of blinding, and study funding whether pharmaceutical industry sponsored or academic or government funded. All the data collected were analyzed using descriptive statistics. SPSS software version 16 (SPSS, Chicago, IL, USA) was used for statistical analysis.

RESULTS

Twenty-one thousand four hundred studies have been registered with the CTRI from its inception year 2007 to August 2019. However, only 99 studies are exclusively for the geriatric age group which account for only 0.46% of the total studies. Out of 99 studies, 60 were interventional studies, whereas 39 were observational

studies. Among interventional studies, 46 (77%) were randomized controlled trials and 14 (23%) were nonrandomized studies. Computer-generated code was the most common technique used for randomization (26), followed by the coin toss method (8). The techniques used for randomization are displayed in Figure 1.

Blinding was done in 36 interventional studies, of which 22 studies were single blind (participant – 15, outcome assessor – 7) and double blinding was done in eight studies [Figure 2].

Out of 99 studies, 60 were postgraduate theses. Eighty-seven trials were investigator initiated, government funding institutes sponsored eight, and pharmaceutical companies sponsored only four. Only two out of 99 were global trials. Concerning distribution across states, Karnataka contributed to the maximum number of studies in the geriatric population (34.2%) and was followed by Maharashtra and Delhi (15.3%). The distribution across various states is represented in Figure 3. Out of all the studies, only nine studies were multi centered.

All the studies had obtained ethics committee permission before initiation. Only four studies had obtained DCGI permission, while the remaining studies stated it as not applicable. Forty-three trials were registered retrospectively in CTRI, whereas 56 were prospectively registered.

The lower limit of inclusion criteria was 60 years in 73 studies, 65 years in 22 studies, and 70 years in one study. The upper limit of the inclusion criteria for was 99 years (in 28 studies). The various upper limits of inclusion are represented in Figure 4. Ninety-four studies had both sexes in inclusion criteria; two studies had only males, whereas one study had females exclusively in the inclusion criteria.

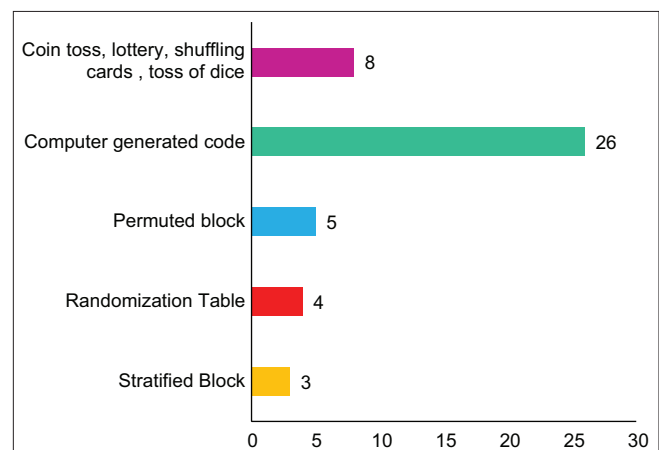


Figure 1: Randomization methods

Neurology (24 studies) was the major therapeutic area that was studied, followed by community medicine (21 studies), orthopedics (15 studies), and anesthesia (10 studies). The distribution across various therapy areas is shown in Figure 5.

Apart from the above, oncology, general surgery, endocrine, ENT, gynecology, and psychiatry were other major specialty areas.

Of all the interventional studies, 17 studies (28%) tested allopathic drugs, 26 (43%) tested a lifestyle intervention, 7 studies (11%) tested a surgical intervention, and the rest were nutraceuticals, Ayurveda, Yoga and Naturopathy, Unani, Siddha, Homeopathy interventions. [Figure 6] The majority of the interventional studies were with two groups (47 studies).

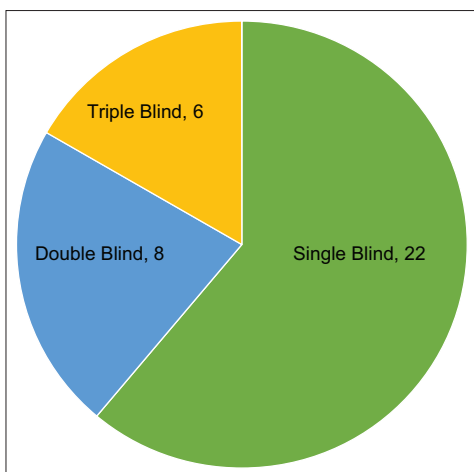


Figure 2: Type of blinding

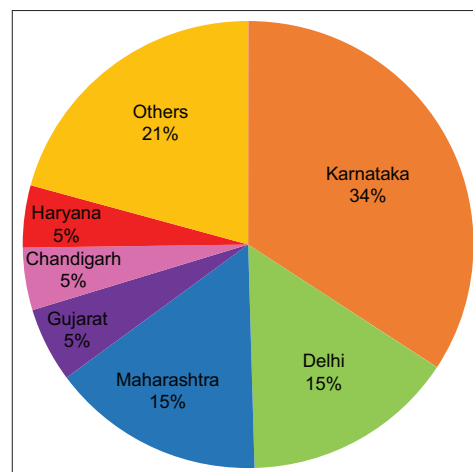


Figure 3: Statewise distribution

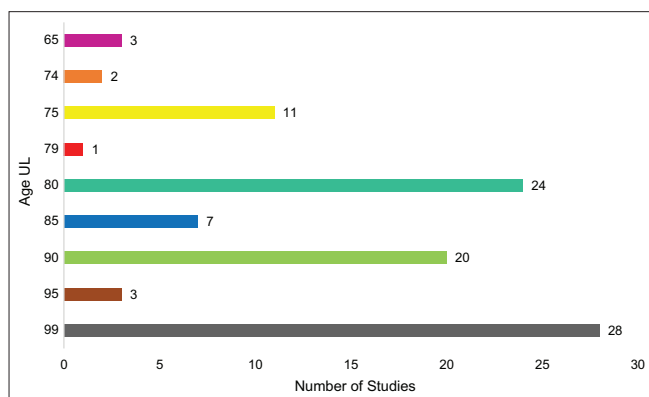


Figure 4: Upper limit of age

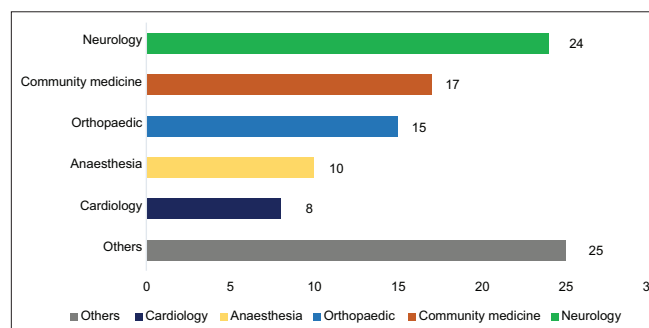


Figure 5: Specialty area

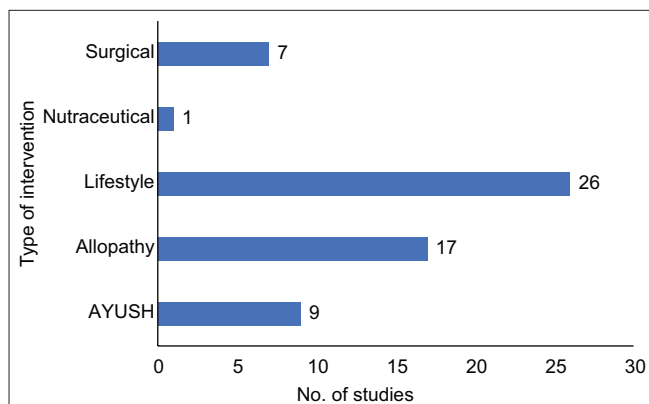


Figure 6: Type of intervention

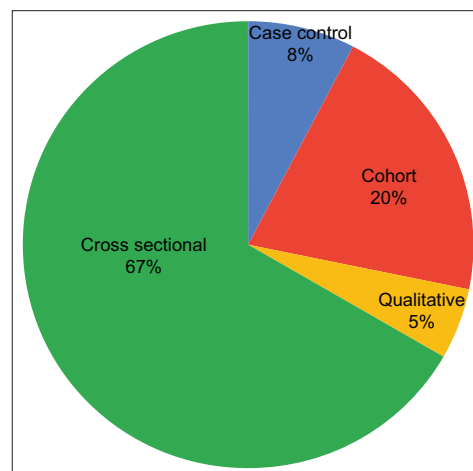


Figure 7: Types of observational studies

Among observational studies, 26 (66.7%) were cross sectional, 8 (20.5%) were cohort studies, 3 (7.7%) case control, and 2 (5.1%) qualitative studies [Figure 7].

Out of 99 studies, 35 studies were completed till the time of analysis, and only ten out of those had published their results either on the CTRI site or in the form of publications.

DISCUSSION

The elderly population in India suffers from a variety of communicable and noncommunicable diseases, which get further compounded by declining immunity and impaired sensory functions. A recent study revealed that about 17.93% of older men and 26.21% of older women in the country experience either mild or severe disability in terms of activities for daily living needed for a better quality of life.^[6] A study conducted in year 2011–2012 revealed the most common disease in the elderly to be hypertension, followed by cataract and diabetes.^[7] Considering the geriatric population's heterogeneity, this study was conducted to give an overview of the research being conducted in them.

The present study showed that <0.5% studies of all studies registered in CTRI were about the geriatric population. The elderly have often been excluded from trials. However, given the change in pharmacokinetics and pharmacodynamics after the age of 75 years, the inclusion of older people needs special attention.^[8] In order to overcome this challenge of underrepresentation, the International Conference on Harmonization (ICH) issued the ICH E7 guideline in 1993 for conducting studies in the geriatric population. It stated that the trial population should reasonably represent the population that will be later subjected to the drug and should include a minimum percentage of older participants. Konrat *et al.*^[9] conducted a study to compare the proportion of elderly patients included in trials of medications that used in this representative population in clinical practice. The study findings revealed that only three out of 155 clinical trials on four widely prescribed drugs were exclusively designed for elderly patients, i.e., 65 years and above. A similar study carried out by Ruitter *et al.* found underrepresentation of the elderly in clinical trials.^[10]

Our analysis revealed that a maximum number of studies were conducted in neurology, followed by community medicine, orthopedics, and anesthesia. Our study findings were in line with earlier studies revealing the underrepresentation of the elderly in clinical studies in cardiology and oncology.^[11,12] Another study which analyzed interventional trials registered on

the Food and Drug Administration website observed the most common disease categories; “Alzheimer’s disease,” cardiovascular and circulatory diseases, “falls and musculoskeletal disorders.”^[13] Our study revealed that two trials were done in males and one in females exclusively. However, the disease population in all the three trials were not gendered exclusive. All the three studies were a comparison of two anesthetic agents in surgeries.

The most common interventions tested as per our study were lifestyle interventions, followed by allopathic drugs. As per the study by Bourgeois *et al.*,^[13] drugs constituted the most common intervention accounting to almost one-third of trials, followed by behavioral (17.5%) and others and devices. Furthermore, this study showed that most studies were open label, followed by single blinding. Our analysis also revealed most studies to be single-blind.

The majority of the studies were investigator initiated, with only four pharmaceutical-sponsored drug intervention studies. In contrast to this, according to the study conducted in the US by Bourgeois *et al.*, 18.9% of the interventional trials in the elderly were industry-sponsored studies.^[13] Another study analyzing the inclusion of older people in clinical trials of recently authorized medicines showed that for diseases not unique to, but present in, old age, <10% of the participants were aged 65 and older, and only 1% being aged 75 and older.^[7] Among research papers published in major medical journals, 30%–40% had excluded elderly people without justification.^[10] Trials of type 2 diabetes mellitus trials also had surprisingly lesser representation of the elderly, even though most people with diabetes mellitus in developed countries are aged 65 and older, 15% are aged 80 and older. The failure to include participants aged 75 and older in epilepsy trials is also striking because one-quarter of individuals with epileptic seizures are aged 60 and older, and more than 10% are aged 70 and older. This signifies that the involvement of the elderly population in trials related to conditions expected in the said age group needs to be focused on.

If we want to practice evidence-based medicine and to base our clinical judgment on firm scientific evidence, it is necessary to design studies that will allow participation of the elderly, and we need to find new ways to increase participation. Regulatory agencies also need to participate actively as the last guidelines released was in 1993. There is also a need for trials focusing only on elderly participants. Many clinical trial protocols include comorbidities in exclusion criteria that lead to disqualifying of older patients.

The Indian government has taken initiative by bringing National Programme for Health Care of the Elderly. However, the implementation of such a program has not been seen on large scale. Few colleges such as All India Institute of Medical Sciences, Grants Medical College and JJ Hospital, Mumbai, and Madras Medical College, Chennai, have started dedicated geriatric OPDS. Only two government medical colleges Madras Medical College, Chennai, and Government Medical College, Aurangabad, have MD geriatric medicine seats. However, there is a need for more outpatient department and specialization seats to cater a large population of the elderly. An emphasis should be made right from the undergraduate curriculum by adding separate sections on “Elderly patients” in all books such as geriatric oncology, geriatric orthopedics, palliative care, and geriatric medicine.

A limitation of the present study was that since CTRI registration is not mandatory for nonregulatory studies, all studies conducted in real time may not have been analyzed. Furthermore, studies which comprised of adult and geriatric population together were excluded.

Interestingly, out of 21,400 studies, only 99 (.46%) were on elderly patients and only 10 studies had published their results making it even further small (0.046%).

CONCLUSIONS

This study depicts the marked underrepresentation of the geriatric population in clinical studies and also highlights the need to conduct more studies in specific areas exclusive to the elderly.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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