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Original Research Article

Assessment of clinical trials registered at clinical trial registry of India over past decade: an audit

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ABSTRACT

Background: Clinical trial registry of India (CTRI) was launched in 2007. In this audit we attempted to assess the clinical research scenario over the past decade by looking at the information about clinical studies registered at the CTRI from 2007 to 2016.
Methods: We accessed the official website of the CTRI i.e. www.ctri.nic.in and the required information was downloaded and descriptive statistics were used.
Results: We found that the number of studies went on increasing from 31 in 2007 to 589 in 2016 and 1130 in 2015 (as on 22nd June 2016). Majority studies were of interventional in nature as compared to observational and bioavailability and bioequivalence (BABE) studies. Pharmaceutical industry sponsored studies were comparatively higher in number than any other sponsored studies. However their number went on decreasing, while increase in registration of post graduate thesis and investigator sponsored studies was observed.
Conclusions: Though a decrease in Pharmaceutical industry sponsored studies was observed the overall clinical research scenario appears to have improved due to investigator initiated studies and post graduate thesis.

Keywords: CTRI, Clinical research, Pharmaceutical sponsored, Investigator, Post graduate thesis, India

INTRODUCTION

Clinical research in India is mainly divided into academic clinical studies and those studies which are funded by Pharmaceutical Industry. Pharmaceutical Industry sponsored data is available from publication in various journals and at http://www.clinicaltrials.gov. However the data of studies undertaken by investigators and post graduate students is not available if not published. Studies which fail to show significant results are not published as many trials get abandoned or not even published due to "negative" or equivocal results by the investigators.[1] Hence in order to establish trust accountability and transparency, the Clinical Trials Registry of India (CTRI) was hosted at the ICMR's National Institute of Medical Statistics (NIMS). It is a free and online public record system for registration of clinical trials being conducted in India. It was launched on 20th July 2007. Initiated as a voluntary measure, since 15th June 2009, trial registration at the CTRI was made mandatory by the Drug Controller General Of India (DCGI).[2]

It was of great interest to find what happened to clinical research scenario in India in this decade. Hence the purpose of study was to conduct an audit of clinical trials registered at the clinical trial registry of India till 22nd June 2016 since the date it was launched.

METHODS

This was a retrospective audit. The study protocol was exempted from review by the Institutional Ethics Committee I (EC/OA-99/2016). The website

www.ctri.nic.in was accessed (last date on 22nd June 2016). The objectives of the study were:

1. To assess the total number of Studies registered at the clinical trial registry of India from its launch to 22nd June 2016
2. To assess the Year wise distribution of studies
3. To assess the nature of studies
4. To evaluate phase wise distribution of studies
5. To assess the State wise distribution of studies
   Individual study was then assessed for:
   a) Type of Sponsorship
   b) If it was Post graduate thesis
   c) Retrospective registration

Additionally we also accessed clinicaltrials.gov site to find the number studies done in India from 2007-2016.

The data was analysed using descriptive statistics.

RESULTS

A total of 7061 studies were registered from the launch till June 2016. Figure 1 shows that the number of studies went on increasing with each passing year. Highest numbers of studies 1130 were recorded in the year 2015. While in the year 2016 the number of studies fell sharply (Figure 1).

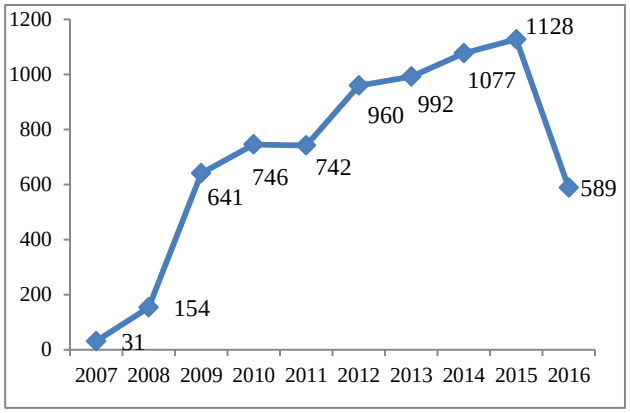

Figure 1: Year wise distribution of total number of studies.

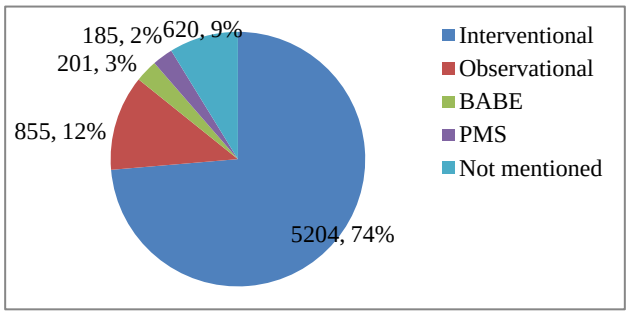

Figure 2: Types of studies.

Of these almost 74% studies were of interventional while 12% were observational and BABE and Post marketing studies were 3 and 2 % respectively in nature as shown in Figure 2. It was found to be missing in 9% studies (Figure 2).

Most interventions belonged to modern medicine while in Phase 2 a considerable number of interventions were of Ayurvedic in nature. Very small number of interventions belonged to Homeopathy and Unani. In others which were also small in number the interventions were cosmetic in nature (Figure 3).

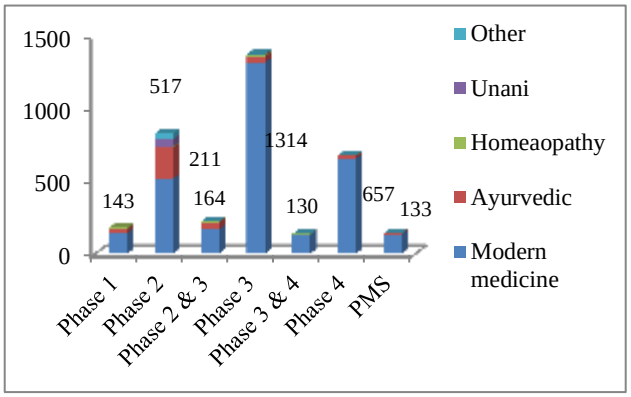

Figure 3: Phase wise distribution of studies done by various systems of medicine.

There were 37% studies were present in Phase 3 followed by Phase 4 (20%) and Phase 2 (19%). While Phase 1, 2 and PMS had least number of studies. However a large number of studies were also present in not applicable (N/A) category which was not defined (Figure 4).

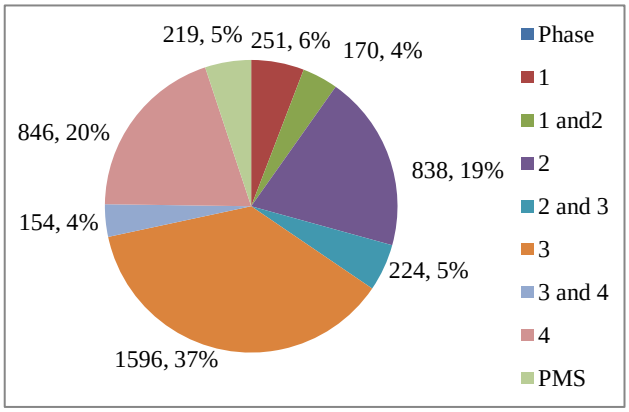

Figure 4: Phase wise distribution of studies Total=4298.

The studies were being conducted at 5625 sites. Maharashtra topped the list followed by Gujrat and Tamil Nadu, Andhra Pradesh and Karnataka. While states like Meghalaya, Arunachal Pradesh, Anadaman had only 2 study sites (Figure 5).

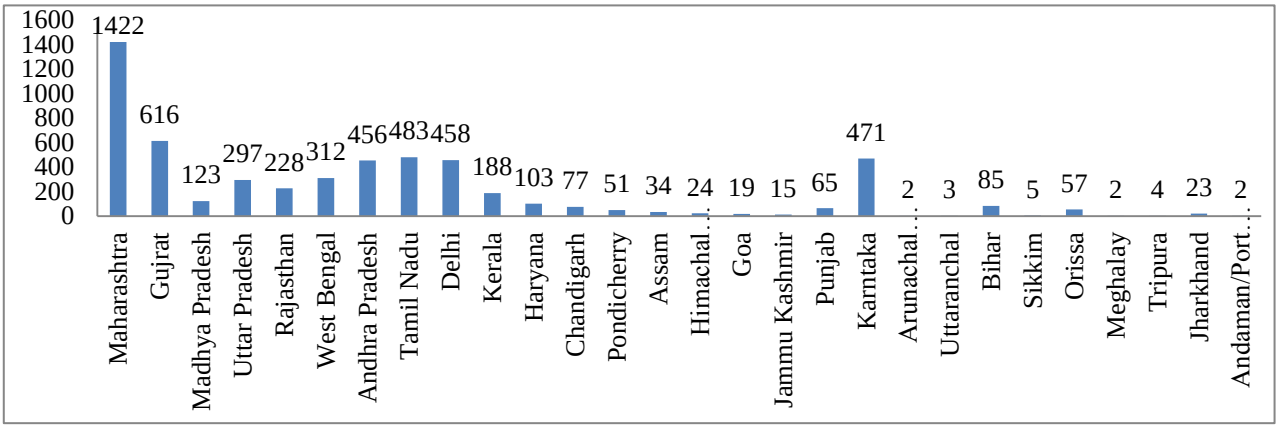

Figure 5: State wise distribution of sites of studies.

The percentage of Pharmaceutical industry sponsored studies was higher as compared government and investigator sponsored. The Industry sponsored studies peaked at 2010 and consistently fell thereafter till 2016. While both government and investigator sponsored studies peaked at 2008, fell in 2009 and then remained constant throughout (Figure 6A). As compared Pharmaceutical industry sponsored studies sponsored by the medical colleges whether private or government and research institute fell in 2009 from then rose till 2016 (Figure 6B).

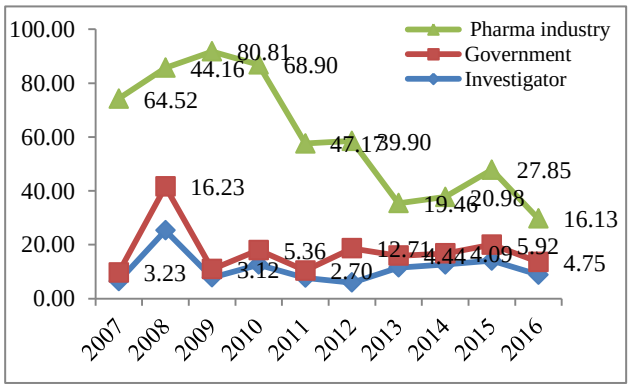

Figure 6A: Sponsorship of studies.

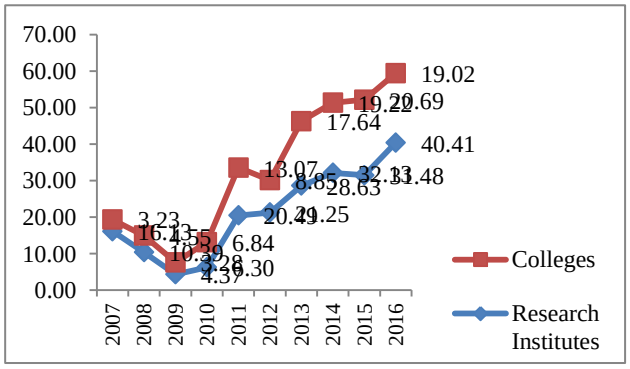

Figure 6B: Sponsorship of studies.

The number of clinical trials registered at clinicaltrias.gov initially rose till 2010 and subsequently fell down from the year 2011 to 2016 (Figure 7).

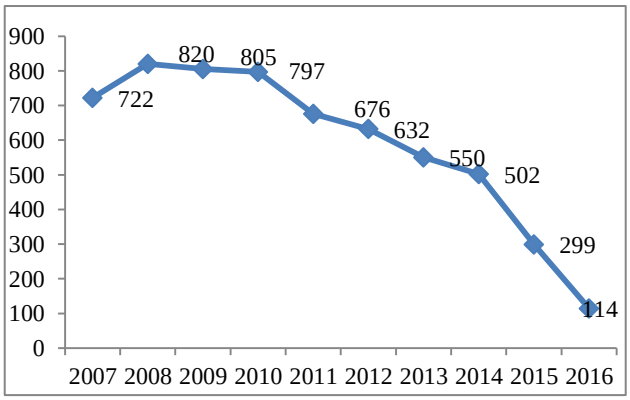

Figure 7: Clinical trials from India registered at clinicaltrials.gov.

The number of studies that were registered retrospectively went on increasing from 2010 till 2015. As of now the number has fallen to 338 (Figure 8).

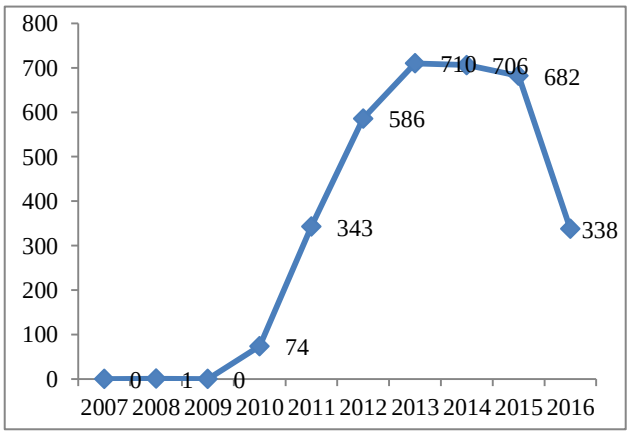

Figure 8: Retrospectively registered studies.

The number of post graduate thesis went on increasing from 2010 till 2015. It appears to have fallen in this year (Figure 9).

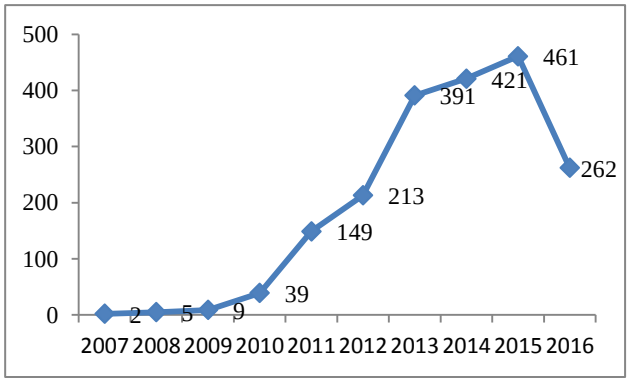

Figure 9: Number of post graduate thesis registered.

DISCUSSION

A gradual but consistent increment in number of overall clinical studies was observed over the past decade. This includes studies apart from modern medicine like Ayurveda, Homeopathy, Unani and few cosmetic studies like patch test.

The regulatory research which included the one that is sponsored by Pharmaceutical industry constituted majority. These studies are governed by Schedule Y of Drugs and Cosmetics Act 1940, Rules 1945 which was first introduced in 1988 and revised in 2005 and was amended from time to time thereafter.[3,4] The Pharmaceutical industry sponsored research appears to be influenced by the regulatory processes. Additionally India which had large pool, low cost availability of expert researchers were favourable.[5] Goldman Sachs, Centre watch, Goldman Sachs and McKinsey in 2008 reported that the Indian pharmaceutical industry is growing at an annual rate of 11 % and the clinical research industry is growing an annual rate of whopping 84 %.

The other complimentary factors were strong availability of study subjects across major therapeutic segments; cost competitiveness, high level of ICH-GCP & USFDA standard compliance, and favourable regulatory climate. In addition 12% Service tax exemption was another point which strongly favoured the multinationals to expand their business in India. The clinical trial applications were approved in record short time of 8-10 weeks for drugs marketed in India.[6] Thus all these helped the Pharmaceutical Industry whether Indian or Multinational to grow and therefore it reflected in peak during 2009 and 2010. However subsequently the number of studies fell. This can be correlated with the fall in studies registered at clinicaltrials.gov. That could be explained by R and D expenditures which fell by MNCs in India from 2007 to 2013 in the following table. It appears abolition of product patent law in the country lead to those consequences.[7]

Table 1: Source-calculated from CMIE prowess database.

Year	Expenditure by MNCs in million rupees
2007-8	438.6
2008-9	563.5
2009-10	570.2
2010-11	325.5
2011-12	246.7
2012-13	337.1

While in 2013 with the release of series of notification related to compensation, SAE reporting, registration of ethics committees and punitive actions for noncompliance for sponsors, the scenario worsened.[8-12] These notifications had a significant impact on not only number of clinical studies, Even the number of approvals of registered clinical trials declined.[13]

Lack of support for research and development is evident from fewer numbers of studies in initial development phases. It is argued if financial reasons or lack of comprehensive indigenous capability is responsible for such apathy.[14] This also brings us to the fact that the research in Ayurveda, Homeopathy and Unani the Indian traditional Medicinal systems have not been explored much and there are no evidence based finding that can be documented. They still rely on ancient text available.

A very encouraging finding was rise in the number of investigator sponsored studies. It is possible that this recorded number may be still lower than actual one as many investigators may not have registered their studies at the registry. This may be reflection of requirement of publication for promotion or genuine increase in the interest of the faculty for research. At the same time we also observed that the number post graduate thesis went on increasing which shows increasing awareness regarding this process among the post graduate students and their teachers. Over a period of years the number of post graduate students must have been increased which has reflected in this. Additionally the responsibilities of supporting these studies have been taken by the Government as well as Private medical Colleges. Research institutes whether Indian or foreign have also supported the studies to large extent. So funds could be created by Government locally at the medical college or research level to speed up funding process. The motive behind launching this registry was that many investigators do not publish their work due to publication bias. This registry will maintain the data of all studies and will be useful for knowing the required information in such situation.

We observed a slight improvement in government sponsored studied during 2012 however at other time it was lower and constant. Very often the funds from government agencies are not available in time and therefore are not spent. We therefore feel that government

bodies may fast track the processes which will greatly benefit investigator initiated studies.

From 2011 we observed rise in retrospectively registered studies although the primary objective was to register the studies prospectively. It is possible that the changing regulatory scenario may have influenced this.

Major sites of studies were Maharashtra, Gujarat, Karnataka and Andhra Pradesh while there were few sites from Arunachal Pradesh, Meghalaya, Andaman and Tripura. All the clinical studies had ethical approval in place. However not all the ethics committees which approved these studies were registered with CDSCO. Our previous study has shown that Maharashtra has highest number of ethics committees registered with CDSCO, but that number is still lower than the number of sites that we have been obtained after removing all duplicates. States like Meghalaya, Arunachal Pradesh, Andaman and Tripura do not have any ethics committee which are registered with CDSCO.

We did not evaluate all data especially completeness of the study details as weel as therapeutic areas covered. But it was observed that many studies were incomplete. These are limitations of our study. There were problems encountered while collecting the data or misunderstanding by investigators who must have uploaded the information, as we found one site/institute name entered by different ways; but the efforts taken for initiating and maintaining this site are considerable and admirable. We also feel clinical trials for Ayurvedic, Homeopathy, Unani medicines and cosmetic trials could be separated from main stream of modern medicine but maintained on the same page.

To conclude despite decrease in Pharmaceutical industry studies, the overall clinical research scenario in the country has improved over the past decade, which could be attributed to investigator, research institutes, medical colleges/hospitals and government funded studies. Taking into consideration increasing number of investigator sponsored studies we feel government funding sources which take time be made easy and fast available so that research in our country is promoted.

CONCLUSION

Month wise study showed that numbers of the non-compliance in prescription audit was reduced from 33 (in the month of December 2012) to 18 (in the month of February 2013). This is mainly due to the hospital management has implemented the suggestion provide by clinical Pharmacist (project trainee) to improve their processes by mean of SPC analysis.

The management of the hospital or Quality committee had focused on results of this prescription audit. In nut shell we can conclude that the process set by the NABH is the robust one and involvement of Clinical Pharmacist & Pharmacologist for in the Prescription audit process is possible which helps the Hospital management during accreditation.

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Ethical approval: Not required

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