**Title**

**Perspective of researchers towards conducting a clinical research**

**Running title**

**Perspective of researchers in clinical research**

**ABSTRACT**

Good Clinical Practice (GCP) guidelines have been introduced in India one and a half decades ago. Limited number of agencies are providing training on GCP, which has caused a number of complexities. The present survey was conducted to assess the attitude of researchers involved in clinical research and to recognize most important topics in GCP training to enhance clinical research.

An online-survey was conducted using surveymonkey. More than 500 researchers were contacted through email. Questionnaire comprising 10 questions included demographic details and questions related to their perceptions and difficulties in conducting clinical research.

A total of 158 participants responded to the survey. Female researchers were less as compared to male researchers. Complicated paperwork (39.2%) and concept of lost-to-follow-up (39.2%) were the major issues for conducting proper clinical research. In the workshop attended, statistical analysis (60.3%), sample size calculation (58.2%), data management (56.2%), how to write a protocol (53.4) and ethics (4.5%) were the most interesting topics for them. Participants indicated that most of the criticisms from reviewers were on sample size calculation and statistical analysis.

Our study results emphasize the need of training on topics of statistical analysis, sample size calculation, ethics and writing of a protocol. GCP training in clinical research with biostatistics may improve the quality of research. Adequate formal training of GCP to all the investigators, managers and data management staff will help to adhere to ethical requirements.

**Keywords**

Good Clinical Practice, Clinical Research, Participants perspective

**Introduction**

Patients and the drug companies get utmost benefits from a successful clinical trial, which may also have an impact on some other stakeholders such as government, regulators, ethics committee, media, community and public. A well planned clinical trial with adherence to robust methodology written in the protocol may give a significant insight to the outcome. Good Clinical Practice (GCP) guidelines are meant for the researchers involved in clinical trials for dealing with human participants in their research. These are also adapted by clinical researchers as ‘best global practice’ so as to ensure them with the confidence that the right, safety and well being of all their human parricipants are well protected and the data derived from such studies are credible and accurate.

World Health Organization (WHO) created scientific group in 1968 to review and formulate principles for only “Clinical Evaluation of Drugs”. Later in 1975, another scientific group was convened by WHO to perceive other aspects of drug development such as guidelines for research including evaluation and development of drug. Finally WHO commenced guidelines on GCP for trials on pharmaceuticals products in 1995 with the purpose of setting globally applicable uniform standards for the conduct of such biomedical research on human subjects1. These Guidelines are addressed not only to investigators, but also to ethics review committees, pharmaceutical manufacturers and other sponsors of research and drug regulatory authorities.

International Council for Harmonization (ICH) which was formely The International Conference on Harmonisation formulated consolidated guidelines on GCP in 1996. The conference was initially hosted by European Federation of Pharmaceutical Industries and Associations (EFPIA) in Brussels in April 1990. Regulatory agencies and industry associations of European union, Japan and the US government worked together to release the GCP guidelines.

ICH defined CGP as *“an international ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety, and wellbeing of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data are credible.”* 2,3.

Latter in 2001, the Indian regulators, Central Drugs Standard Control Organization (CDSCO) launched Indian GCP guidelines developed with consideration of WHO, ICH, USFDA and ICMR - Ethical Guidelines for biomedical research on human subjects. In continuation, CDSCO has taken remarkable step by launching online registry system as Clinical Trial Registry - India (CTRI) in July 2007 to ensure accountability, transparency and information sharing on clinical trials making it available on the public domain4.

The purpose of GCP guidelines of ICH and CDSCO was to regulate the clinical trials however WHO-GCP is more towards guidance to professionals involved in clinical trials.

Clinical Development Services Agency (CDSA) is putting efforts to develop and enhance clinical research capacity in India at par with international standards through a comprehensive training program designed to create a pool of professionals capable of conducting high quality clinical research and trials for epidemiological studies, community outreach and regulatory approvals. CDSA has conducted more than 30 GCP training programs throughout the nation till July 2018. GCP training team at CDSA consists of experts from various areas of regulator, ethical committee, investigator, sponsor, quality control and biostatistician. Strengthening the investigator through GCP training may definitely minimize the misconduct of clinical research.

A pilot survey was done by CDSA in 2015 on 65 investigators who involved in clinical research with aim to know their knowledge on data management and statistics. The result revealed that 67% of the investigators participated in the survey, approach statistician at the time of data analysis. There was no involvement of a statistician from the beginning of the study. 57% investigators were using MS-Excel for data entry and did not know about the 21CFR part 11 (guidelines of keeping electronic record). Most of the investigators analyze data by themselves and 88% chooses statistical software based on easy-to-use concept rather validated one. 31% participants do not know about the assumptions of statistical methods and apply any method as they found suitable to get significant p-value.

Keeping above results in mind, the present survey was planned to know the impact of GCP training and attitude of clinical researchers towards research as there is need of a powerful and mandatory training programs.

**Material and Method**

A cross-sectional survey was conducted using online survey powered by *SurveyMonkey.com* from July through Septemble 2017 among researchers/scientists/clinicians/fellows. Around 500 researchers from various departments were contacted through email those were in contact database of GCP trainings of CDSA. Researchers requested to forward the survey link to their colleague who are involved or conducted research in past to take part in this survey. Questionnaire was designed with reference to Sumi et al (2009)5 with added questions. The structured questionnaire was used with closed ended questions including demographic data, understanding GCP and related problems conducting a research. Questionnaire contains of 10 questions. Questionnaire kept anonymous to gather unbiased information. It was not necessary to take consent from participants for this study as per the Ethical Guidelines for Epidemiological Research6.

As most of the information collected was in the form of multiple choice questions, descriptive data was presented in the form of frequencies and percentages. Chi-square test was used to check association between two categorical variables as appropriate. P-value of less than 0.05 was considered to be statistically significant. Data has been exported in the MS-Excel format and SPSS v23.0 was used to analyze data.

**Results**

Total 158 scientists/clinicians/researchers/fellows participated in the survey. The average time to complete the survey was 4 minutes and 8 seconds calculated by *Surveymonkey* for all responses. Table 1 represents participant’s characteristics. Participant’s cohort was of young researchers of age 30 – 40 years (30.1%) followed by 40 – 50 years (28.2%). There was gender bias found in study group (p-value 0.0274). 59% participants were male. 65.4% of the researchers did not write protocol independently. 54.5% participants have got more than five publications in index journals (ranging from 5 to 67). 65.4% of the participants knew about Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects. Maximum number of participants was from medical/clinical (31.4%) background followed by science & technology (19.9%).

Figure 1 demonstrates the age-gender distribution of participants. Female involvement in research was less in the age group of 30 – 40 years (23.9%). Figure 2 shows the status of researchers participated in this survey. 87.3% participants were currently engaged in research activities however 7.4% will be looking for designing research studies in near future.

Participants were asked regarding the difficulties met of conducting a clinical research (Table 2). Complicated paperwork and many lost-to-follow-ups were the most frequently quoted difficulties, and was mentioned by 39.2% participants followed by time limitations. 33.1 % respondents felt that there are monitoring issues in conducting clinical research. Table 3 describes summary of a question asked to participants regarding whether lecture topics related to clinical research are interesting or useful. Most participants (60.3%) thought that lecture on statistical analysis was useful followed by sample size calculation (58.2%). However lecture on data management was also liked by 56.2% participants. Other than technical sessions, lectures on writing protocol (53.4%) and ethics (44.5%) were found useful in conducting clinical research and appreciated by respondents. Most frequently cited criticisms of a reviewer when submitted manuscripts for publication were on sample size (29.3%) and statistical analysis (28.5%).

**Discussion**

In the present study, most of the participants were currently involved in clinical research. Women aged between 30 – 40 years were less involved in research. The reason for this might be because of family comitements. Gender bias was statistically significant in this study. Our finding reveals that complicated paperwork and concept of lost-to-follow-up were the most frequently quoted difficulties in conducting clinical research. Some other studies also indicate the same results 5,7,8.

Studies have reported5,15 that statistical analysis, sample size calculation and data management were the most useful lectures. Our study endorses there observations. Young researchers would like to learn statistical concepts involved in writing a protocol and appreciated it in GCP training. However very few respondents (5.4%) thought that there is no need for statistical topics in GCP training. Our survey confirmed that the difficulties faced by participants in conducting clinical research are same as those reported in the previous studies 10,11,12.

Participants who were GCP trained earlier were better responders in answering the assessment form than those who were not, as they would have developed the skills because they were aware of the guidelines14,15,16,17.

Majority of participants responded that the reviewer’s most common criticism was on sample size calculation, statistical analysis and aims and objectives. Proper planning, designing and compliance to the research protocol will definitely check misconduct and reduce errors in conducting a clinical research. This result is similar to a study which showed that physicians need more administrative assistance and greater knowledge of the principles and techniques of clinical research, especially the concepts of biostatistics2.

**Conclusion**

GCP trainings are having good impact on clinical research especially if technical topics such as biostatistics are involved in it. Our study results emphasize the need of topics of statistical analysis, sample size calculation, ethics and how to write a protocol. GCP training in clinical research with biostatistics may improve the quality of research. Adequate formal training of GCP to all the investigators, managers and data management staff will help in ethical conduct of clinical research. There is need to make GCP training mandatory in all medical institutions conducting research whether it is government sector or private.

**Limitations**

There were some limitations in the present study. Since the participants were from different background - researchers, clinicians, physicians, scientists, biostatisticians – emphasis on different topics for training were suggested. Low number of responses (26.4%) could not provide a proper direction for further training.

**Conflicts of interest**

*None of the authors have conflicts of interest to manuscript*.

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