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Original Article

Pharmacology Section

Knowledge and Attitude Towards the Translation of Medical Research to Clinical Benefit Amongst Researchers in A Tertiary Care Hospital

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ABSTRACT

Introduction: One of the primary goals of any biomedical researcher should be practical applicability or the translation of scientific discoveries to clinical care. Research that lacks potential for translation contributes to ineffective use of resources, time and manpower. Hence, it is important for researchers to be aware that the clinical significance should not be forgotten in the quest for a significant p-value.

Aim: To assess the knowledge of researchers in ascertaining the practical applicability of his/her own research, to ascertain their motives in planning research and to evaluate the attitude of researchers towards the ethics of doing research that is less likely to translate into clinical benefit.

Materials and Methods: This cross-sectional study was conducted at a tertiary care medical college hospital in South India. Teaching faculty from clinical, pre and para-clinical departments were administered a questionnaire which included 14 questions. The questionnaire consisted of five knowledge and nine attitude questions. The responses were analysed qualitatively and expressed as frequency distributions.

Results: A total of 60 researchers were included and given the questionnaire. The respondent rate was 32 (53.3%). Only 3 (9.4%) were completely aware of "translational research" while about 11 (34.4%) knew that research done by pre and para-clinical sciences could be both basic and translational. Also, 17 (53.1%) of participants were willing to do research that did not result in either immediate or direct clinical benefit. A small minority of 4 (12.5%) admitted that the focus of their research was to achieve statistical significance. About 10 (31.3%) of researchers surveyed and felt that research offered an opportunity for free treatment to patients and 5 (15.6%) felt that therapeutic misconception was acceptable.

Conclusion: This study identified the gap between knowledge and understanding of the practical applicability of research and its ethical perspectives amongst researchers and hence, indicates the need for increasing awareness on the importance of assessing the translatability of one's research.

Keywords: Clinical significance, Ethics, Practical applicability, Statistical significance

INTRODUCTION

In the current era, there is a substantial increase in the number of researches done and published. The current system of publication in biomedical research provides a distorted view of the data generated [1]. There is too much focus on statistical significance, with parameters more important than statistics fading into oblivion [2]. The primary goal of any biomedical researcher should be practical applicability which refers to the translation of the scientific discoveries to clinical care [3]. Translational research refers to transfer of knowledge from bench to bedside [4].

Biomedical research tends to be skewed as most data generated are positive and mushroom around a particular topic at a particular point in time [1]. When a researcher looks to find solutions for his or her own clinical problems, research is done with a practical end point in view. However, when there is no room for this, research tends to lose quality.

Improper study designs waste resources and generate results that are not strong enough to translate to clinical practice. Small effect sizes are chosen to generate statistical significance more readily [5]. However, statistical significance is not the same as clinical significance and this tends to be forgotten in the quest for a 'significant' p-value [2]. From an epidemiologist's perspective, the relevant question is whether the study's hypothesis is true i.e. the probability of the hypothesis being greater than 0.05? For clinicians, the relevant question is whether a particular strategy can be followed in an individual patient or a subset of similar patients [6].

We believe that it is also unethical to expose the patient or healthy volunteer to any risk, however, small or theoretical, if it does not have the potential to benefit him and/or society. So, this study was designed to evaluate the knowledge of the researchers in assessing the practical applicability of his or her research in future patient care. Secondly, the study also aimed to ascertain the motives of the researcher towards doing research and to evaluate the attitude of the researcher towards the ethics of doing research which is less likely to translate into clinical benefit.

MATERIALS AND METHODS

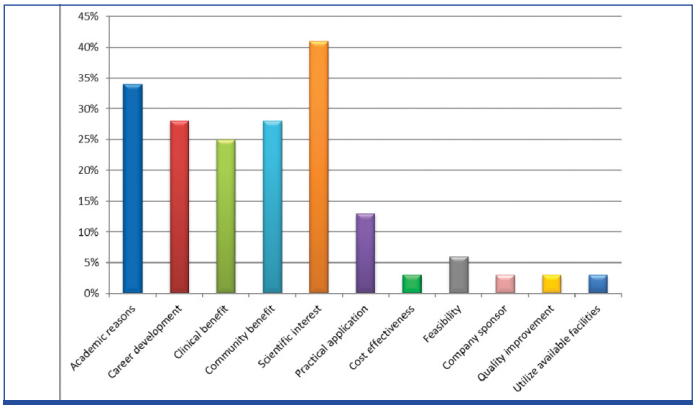
This cross-sectional study was done after the approval of Institutional Human Ethical Committee (Approval number: 13/250) for six months from November 2014 to April 2015. Teaching faculty of our tertiary care and teaching hospital in Coimbatore, Tamil Nadu, India was surveyed with a questionnaire to evaluate their knowledge on assessing the practical applicability of their research and their attitude towards the ethics of research lacking the potential for translation. The study participants recruited were teaching faculty who had involved in research while postgraduates, residents and faculty who had not done any research were excluded.

The questionnaire consisted of 14 questions, of which five were knowledge questions and the remaining were attitude questions. The questionnaire was drafted to be self-administered and it was validated by a team of three members who were researchers belonging to the three levels namely, Assistant professor, Associate professor and Professor; thus representing three different strata with reference to both the quantum and experience in research. Reliability analysis done using SPSS software revealed a cronbach's alpha value of 0.797. After obtaining a written informed consent from each participant, the questionnaire was administered. The responses were qualitatively analysed and expressed as frequency distribution of percentages. Detailed statistical analysis was deferred to enable meaningful expression and lucidity of inferences from the qualitative data.

RESULTS

Out of 60 researchers, who were included for the study and given the questionnaire, only 32 responded by returning the completed questionnaire. Out of 32 teaching faculty who participated in the study, 16 (50%) were Professors, 8 (25%) Associate Professors and 8 (25%) were Assistant Professors. The rest either returned an unfilled questionnaire or failed to give it back. Thus, the respondent rate for the study was 32 (53.3%) and the reasons offered by most for non-participation was lack of time and interest.

There were varied qualitative responses from the participants to the first question on three motives for research. The research intentions were categorized based on the responses specified into 11 categories. It was found that majority had indicated scientific interest 13 (40.6%) and academic endeavours which



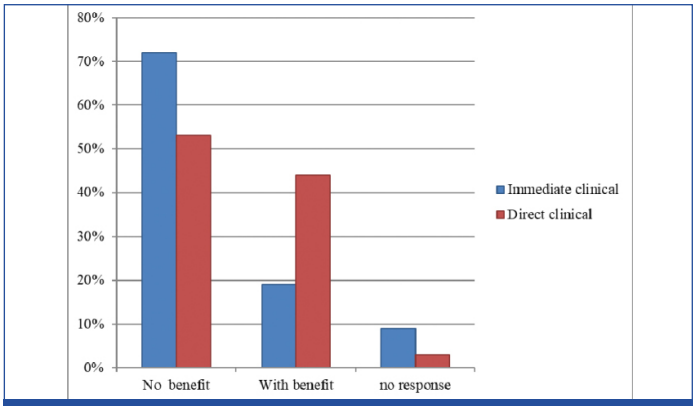
[Table/Fig-1]: Motives indicated for research (%).

included guideship responsibilities, interdisciplinary research, or mandatory involvement in clinical audits 11 (34.4%) as the driving forces in their research involvement [Table/Fig-1].

It is fundamental for the researchers to be familiar with the term "translational research" which denotes translating knowledge from basic sciences to clinical studies as well as translating clinical trials to everyday practice. On this perspective, it was found that the understanding of what translational research means was incomplete; 24 (75%) of participants were partially aware in contrast to mere 3 (9.4%) with complete knowledge about this term. The rest were totally unaware of translational research indicated by their lack of response.

In addition, assessment of the knowledge on research done in preclinical and paraclinical departments, structured as a dichotomous true/false question, revealed that only 11 (34.4%) of participants were aware that research done in pre and para-clinical sciences could be both basic and translational.

Also, 17 (53.1%) of participants were willing to do research that did not result in direct clinical benefit and 23 (71.9%) of them

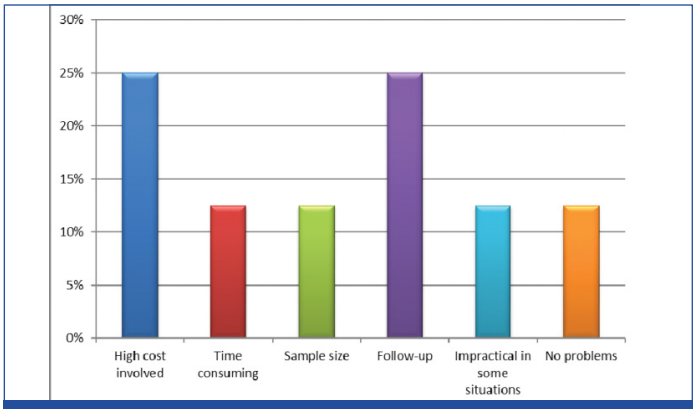


[Table/Fig-2]: Attitude towards doing research and its clinical benefit (%).

opined that their research would not have immediate clinical benefit [Table/Fig-2]. In appraising the attitude of the researchers towards the outcome of testing their hypothesis, a small minority of about 4 (12.5%) admitted that the focus of their research was to achieve statistical significance whilst the rest ascribed that their primary aim in research was to confer greater importance to the clinical significance 10 (31.3%), practical applicability 11 (34.4%) while 7 (21.9%) were in favour of analysing the results irrespective of the statistical significance.

A couple of knowledge questions on sample size and Randomized Clinical Trial (RCT) design revealed that 24 (75%) were aware that smaller the sample size in a study, more likely the research findings cannot be relied upon. On the other hand, the remaining 8 (25%) were unaware of the fact that the sample size could influence the research outcome, out of which 1 (3%) had opted not to answer the question on sample size.

An estimate of only 8 (25%) had the experience of being involved in a RCT and only to this fraction of the study population was the question regarding experiential knowledge on the problems faced during the RCT was directed. The difficulties that they had enumerated included cost, time, achieving the required sample size, follow up of the participants and the impracticality of



[Table/Fig-3]: Problems in doing RCT (%).

addressing certain hypothesis using RCT design. Amongst these responses, cost and follow-up issues ranked highest with 25% each [Table/Fig-3].

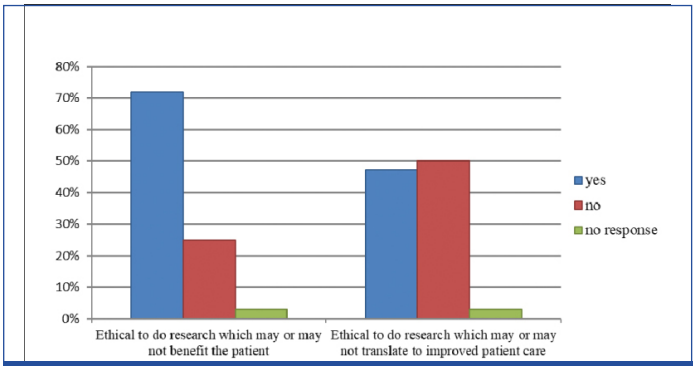
In assessing the attitude of those not having done any RCT 24 (75%), the reasons offered by a greater percentage of participants were that RCT design was not applicable to their research 3 (12.5%) and that they were apprehensive on the difficulties in the conduct of a randomized study 3 (12.5%) whilst 4 (16.7%) revealed that they had not such an opportunity. Two (8.3%) attributed it to practical constraints. The rest indicated lack of motivation.

A rating scale to assess the frequency with which the researchers evaluated the practical application of their research, before

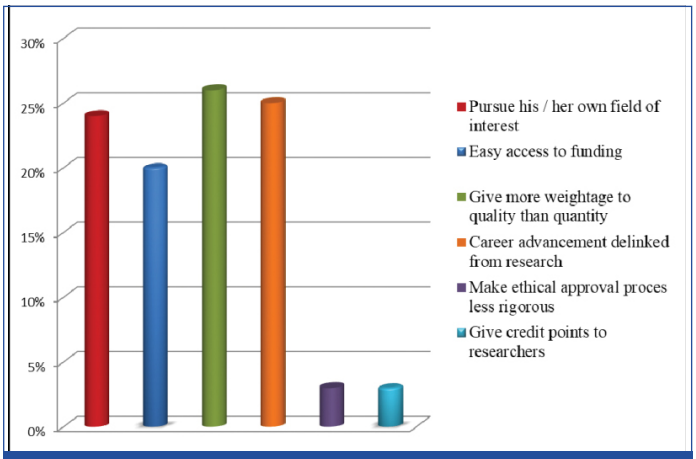
formulating their hypothesis demonstrated that 11 (34.4%) did so "always" and an equal percentage admitted that they did such an evaluation "most of the times."

Interrogating on the ethical aspects, 23 (71.9%) researchers divulged that it was ethical to do research which may or may not directly benefit the patient. Surprisingly, 15 (46.9%) agreed that it was ethical to do research which may or may not translate to clinical benefit [Table/Fig-4].

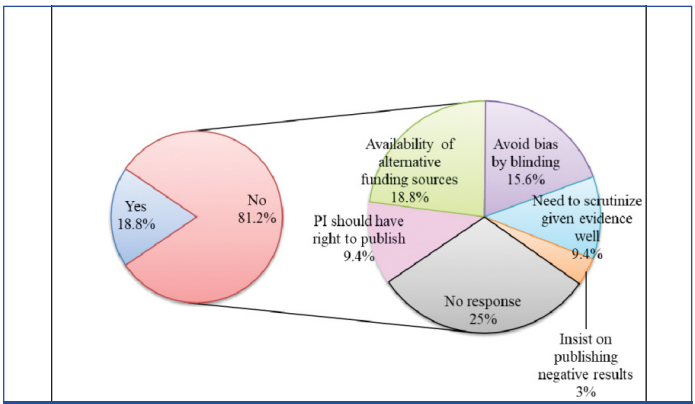
A large majority of study participants 25 (78.1%) opined that the current "publish or perish" situation was unhealthy for translational research. A valid list of strategies identified for improving translational research which most voted for, were



[Table/Fig-4]: Attitude towards research ethics (%).



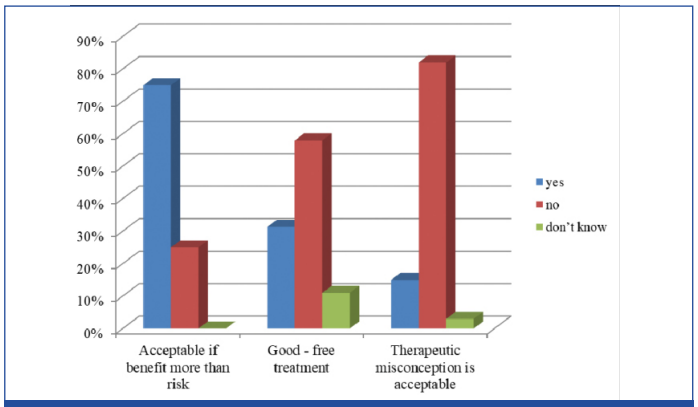
[Table/Fig-5]: Strategies to improve translational research (%).



[Table/Fig-6]: Research in collaboration with drug companies is always healthy (%).
PI - Principal Investigator

to give greater significance to quality than to the quantity of research, allowing one to pursue his/her own interest, delinking research from carrier progression and enabling access to easy funding [Table/Fig-5].

Twenty five (81.2%) were convinced that research in collaboration with drug companies was unhealthy due to a variety of reasons [Table/Fig-6]. Those who felt otherwise 6 (18.8%) did so because such collaboration enabled research, offered funding source, provided easy compensation and facilitated achieving a larger sample size. Twenty four (75%) opined that research which attributed some risk to an individual research subject or a group of research subjects was acceptable only if the possible benefit



[Table/Fig-7]: Questions regarding attitude towards certain aspects of research (%).

to the community was large. It was shocking to discover that 10 (31.3%) felt that clinical research offered an opportunity for free treatment to patients who enrolled themselves in the trial and 5 (15.6%) felt that therapeutic misconception was acceptable [Table/Fig-7].

DISCUSSION

Translation of basic medical research refers to the transfer of new understanding of disease mechanisms gained in the laboratory into clinical care [4]. Though, there are studies on various perspectives of translational research, ours is the first study done to assess the knowledge and attitude of researchers towards translational value of their research findings. The study has brought out that there is only incomplete understanding on translational research and in addition, a high percentage of study subjects were unaware that research in pre and para-clinical departments could be both basic and translational.

It is important for all academic researchers to be aware of "translational research" terminology [7] as they are one of the important stakeholders who are committed not only in identifying and confirming novel concepts through appropriate research, but are also involved in validating the potential of new discoveries to translate to clinical application and improving therapeutic outcomes, thereby culminating in better patient care [8].

In spite of the fact majority of participants have indicated scientific interest as the motive for research, an equally high percentage have revealed that their research endeavours, was part of the academic requirement and was on account of career advancement [Table/Fig-1]. Linking career advancement with the number of publications is indeed a double edged weapon since it motivates the basic scientists and clinicians to undertake more research, thereby promoting research activities; however, the same may not always be true from a translational perspective. This is reflected by a high proportion of study participants disfavouring the "publish or perish" standpoint prevailing as it is unhealthy for translational research.

Clinical evidence of efficacy relies on the dissemination of research results, usually by publication in medical journals which is a critical step that would impact further progression of the research findings [9]. A recent review identified 101 articles published in six top basic science journals which had an apparent promise for development as a major clinical application and yet

only five of these promising advances has been licensed for clinical use over a period of 20 years; out of which only one had created a major impact on medical practice. Three quarters of the promised interventions from basic science papers do not proceed to randomized trial. The article also reported that the strongest predictor of moving to randomized experimentation was industry involvement in the original basic science publication [10].

Science is subject to great uncertainty. An empirical evaluation of the 49 most-cited papers on the effectiveness of medical interventions, published in highly visible journals in 1990–2004, showed that a quarter of the randomized trials and five of six non-randomized studies had already been contradicted or found to have been exaggerated by 2005 [11].

The plethora of scientific information gained through research, promoted largely by academic requisite for career advancement, coupled to limited venues for publication (journals with sufficiently high impact) are factors which deter research in the translation path. Moreover, the current system of publication further perpetuates the publication bias [1]. The more extreme, spectacular results indicating large treatment effects are preferentially published as is evident from the paucity of negative data which are more difficult to get published [12]. The abundance of positive findings published in scientific journals marks the tell-tale effect of selective publishing which not only hampers translation of research findings but also questions the discriminating value of the statistical significance [12-14].

In-depth knowledge of the researchers on the sample size and the relevant design for the research hypothesis is warranted. A study done analysing 215 two arm parallel group RCT of superiority with a single primary outcome published in six high impact factor general medical journals between 1st January 2005 and 31st December 2006 revealed that 5% of reports did not have any sample size calculation and the difference between the sample size reported in the article and the replicated sample size calculation was greater than 10% in 30% of the 157 reports that gave enough data to recalculate the sample size [15]. Thus, every component of a RCT is important for its success; if the design or sample size is inappropriate, then the results of the study will be unreliable, however, well the study is conducted [16].

As it has been rightly highlighted by many participants, there are a number of constraints for conducting RCT which is considered as the gold standard for interventional studies. Apart from implementation issues, complexity involved in understanding the level of clinically meaningful improvement, the expected variation of improvement in the sample, high dropout rates during follow-up are other disadvantages which hinder the choice of RCT design by researchers [17].

The study has made it obvious that researchers are apprehensive about industrial collaboration despite some advantages like the easy access to funding for the conduct of the trial, alleviation of difficulties in providing compensation, use of high quality methods [18] and potential for publication in high impact journals [19]. Nevertheless, industry funding and collaboration in trial design, data collection and analysis have been found to be associated with an increased likelihood of reporting a positive primary outcome and decreased prospect of reporting of trial limitations. Collaborative trials more commonly use surrogate primary endpoints which may, in part, explain why these trials are more likely to have positive primary outcomes [20]. Thus, our results signify that researchers are concerned with interference and influence of the study results and its dissemination by the sponsoring company.

Yet another remarkable finding established is that there is inadequate understanding on the ethical concepts of research as well. Though, ethical challenges for translational research remains the same as clinical research, it should be realized that considerable difference do exists as clinical research is regarded to be ethically distinct from medical care, while translational research emphasizes the links between the two, showing how both need to be grounded in the ethics of doctor-patient relationship [3]. Thus, there is requisite for a different approach towards translational research ethics which reaches farther beyond the research ethics and medical ethics [21]. This study has implied that it is clearly essential to impart ethical concepts to researchers to augment their understanding on ethical principles governing research.

LIMITATION

The major limitation of this study was the small sample size and limited experience of the researchers in RCT designs or trials with industry collaboration. A multi-centric design involving a large sample size from different tertiary centers and medical colleges across India will enable to capture a broader picture of the challenges to translational research.

CONCLUSION

The study has delineated the need for rigorous implementation of educative programs for all researchers to enhance their understanding on the significance of ensuring the practical applicability or translatability of research in addition to improving their knowledge on ethical perspectives. Ultimately, research should be aimed at finding solutions to the everyday clinical problems inorder to have a greater practical end point in view.

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