Ethical review in Pakistan: the credibility gap

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Abstract

The concept of mandatory ethical review of research involving human participants is gradually taking root in Pakistani institutions. Based on the opinions of Institutional Review Board (IRB) members from institutions across the country, the process faces several challenges which threaten its integrity. The lack of registration or accreditation for IRBs has resulted in a wide variation in the calibre and working of such Boards. Despite the recent growth in numbers of people with formal bioethics degrees in the country, a majority of membership remains without any formal training for the work expected from them in ethical review. External pressures to influence deliberations, conflict of interest issues within board leadership and inconsistent application of review requirements all contribute in undermining the reliability of the process. Some of the most significant threats to independent and uninfluenced functioning of such boards arise from institutional leadership itself. In the opinions of IRB members, the review process has to be uniform, consistent and trustworthy if it is to gain the respect of researchers, and IRB need to be given the autonomous space to make independent decisions. Otherwise there is a real danger of IRBs being relegated to being no more than rubber stamping committees.

Keywords: IRB, Bioethics degrees.

Introduction

The concept of ethical review of research involving human subjects is gradually gaining popularity in Pakistan. It however still faces several daunting challenges, some of which threaten its credibility in the country. This paper briefly outlines the evolution of ethical review internationally, and describes the current status within Pakistan. It then addresses the challenges to ethical research in the country based on the deliberations by members of Institutional Review Boards (IRB) from across Pakistan at a workshop held in November 2011 at the Centre of Biomedical Ethics and Culture (CBEC) of the Sindh Institute of Urology and Transplantation (SIUT) in Karachi. To the best of the authors' knowledge, no such report discussing the challenges to ethical review has emerged from the country.

Historical perspectives:

The necessity of human experimentation for medical advancement has always raised ethical concerns, but before the latter half of the 20th century conducting, research was mostly a matter of personal integrity. The concept of ethical review of research involving human subjects by a neutral party originated primarily in the USA. In 1974, with the passage of the National Research Act in America, the National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research was established and led to the 1979 Belmont Report. This document still provides basic guidance for such research in the USA.[1]

On the international front, the Declaration of Helsinki by the World Medical Association in 1964, and the Council of International Organizations of Medical Scientists (CIOMS) guidelines in 1982 were two prominent documents. Each has undergone subsequent revisions and updates.[2,3]

However, despite guidelines, codes and public discussions about exploitative research, the history of human subject research is haunted by scandals of gross abuse of human subjects, some of which have been reported in scientific journals as well as in the lay press. A seminal article by Henry K Beecher published in New England Journal of Medicine (NEJM) in 1966 outlined 22 instances of research abuses in the USA.[4] In the UK, Maurice Pappworth published a series of letters titled "Human Guinea Pigs, a Warning" in 1962 followed by a book in 1967, all of which have had a significant impact on ethical review processes.[4-6] The Tuskegee Syphilis Study on African-Americans which started in 1932 and was brought to a halt only in 1972 has also left a lasting impact on human subject research.[7]

In many developing countries the advent of IRBs was largely due to the globalization of research and the North to South outsourcing of clinical trials, especially pharmaceutical funded trials.[8] A related factor was to maintain eligibility for foreign grants that require the applicants' institutions to provide evidence of ethical review. To this end, the US National Institutes of Health (NIH) through the Fogarty International Centre offered funding for a series of research ethics training initiatives aimed at capacity building in

research ethics in developing countries.[9]

Research Ethics and Pakistan:

The earliest research ethics committee in Pakistan dates back to 1987 but the establishment of IRBs in Pakistan remained a rarity until 2004.[10] Recent years have however seen a steady increase in the numbers of IRBs, some of which are also registered with the US government Office of Human Research Protection.[11] Even in the absence of formal government directives, this growth in Pakistan indicates a cognisance by institutions of the importance of such processes for fostering international collaborative research, obtaining research funding and publishing in reputable journals.

Participation by healthcare providers in sporadic research ethics workshops led to the cultivation of broader interest in bioethics. Between 2001 and 2005, several physicians availed training opportunities overseas through various international Fellowship and Masters programmes funded by the NIH. Some have returned to contribute to developing indigenous graduate level bioethics education programmes within Pakistan.

In 2006, Pakistan's first bioethics education programme, a Postgraduate Diploma Program in Biomedical Ethics, was inaugurated at the Centre of Biomedical Ethics and Culture, SIUT, a public sector organization.[12] This was followed by a Master of Bioethics program at the same institution in 2009. In the private sector, the Aga Khan University (AKU), funded by an NIH grant started a Master of Bioethics program from 2008. According to the information available on the CBEC website, and from personal correspondence with the Programme Director of the AKU bioethics programme, at the time of writing of this paper, there are 135 people who have either already obtained, or are in the process of obtaining graduate degrees in bioethics through Pakistan based bioethics programmes. Many of them are currently serving in various capacities in different IRBs

However, even with an increase in bioethics trained personnel and a gradually rising number of IRBs in Pakistan, there are no registration, accreditation or regulating processes in place. In 2004 the government established the National Bioethics Committee (NBC) Pakistan under the Ministry of Health with the mandate to "promote and facilitate ethical health services delivery, health research and to be an umbrella body linked with the Ethics Review Committee in various organizations/institutions".[13] There is little evidence that the goal has been achieved and IRBs around the country remain islands unto themselves without oversight by NBC. Up till recently, clinical trials in the country required approval from the Drug Control Authority of the Ministry of Health, but even this bureaucratic process has been halted after the recent devolution of the Ministry to the provinces in June 2011.[14,15] In a recent move the National Control Authority for Biologicals, established under the Drug Regulatory Agency of the Ministry of National Regulations and Services has been made responsible for the approval of clinical trials.[16]

Responding to a stem cell research scam in Karachi, the NBC did produce a guidance document pertaining to stem cell research in the country, but here there are no general national guidelines for conducting ethical research.[17] Pakistan Medical and Dental Council (PMDC) Code of Ethics includes a section on research ethics, stating that it "endorses" the Declaration of Helsinki and that this code shall be "binding on all medical and dental practitioners."[18] However, the PMDC is not mandated to regulate human subject research in the country.

Deliberations at the workshop: Practical challenges to ethical research in Pakistan:

A National Workshop on "Strengthening Ethical Review Committees in Pakistan" was conducted at CBEC-SIUT Karachi in November 2011 with collaboration from the Eastern Mediterranean Regional Office of the WHO and Pakistan Medical Research Council (PMRC). Twenty four participants from all four provinces shared their practical experiences of the review process.

Many participants believed that despite the growth of IRBs, all research involving human subjects was still not being submitted for ethical review. This issue is not unique to Pakistan and others have reported similar findings. According to one study "Forty four percent of the respondents reported that their studies were not reviewed by a developing country IRB or Ministry of Health".[19]

According to workshop participants, in addition to human subject research circumventing ethical review, the quality and integrity of IRB reviews that do take place also raise several concerns. They opined that there was a real danger of these bodies being regarded as "rubber stamp committees" with no moral standing if such trends were not addressed. The workshop participants emphasized that the review process had to gain credibility in order to be acceptable to the researchers. They felt that IRB proceedings need to be transparent with well-publicized Terms of Reference, and a simple and consistent application procedure.

Some of the challenges to the review process raised during the deliberations by the participants are discussed below.

Conflict of interest:

Conflict of interest (COI) arising from financial relationships between IRB members and sponsors, especially from the pharmaceutical industry are well documented.[20,21] In addition to financial COIs, there can be a number of non-financial reasons leading to COI as well.[22] The conference

deliberations revealed some of the challenges of COI in the Pakistani context.

An institutional head like the Dean or the Vice Chancellor chairing the IRB has an inherent COI. This is due to the fact the research grants bring funding and prestige for the organization, and an institutional head chairing the IRB would find it extremely challenging to facilitate unbiased ethical review which may potentially block lucrative funding opportunities for the institutions he or she heads. Data presented by the PMRC representative at the workshop based on a nationwide survey of IRBs associated with medical schools revealed that out of the 58 responding institutions, over 80% reported that their IRB was chaired by the institutional head. The common rationale presented by the institutions for this arrangement was that it added to the strength and stature of the board. Conference participants expressed their helplessness in challenging this practice, citing the culture of hierarchy in the country.

Inconsistent review process:

Workshop participants reported that researchers at their institutions were often unaware of the necessity for an IRB approval. This resulted in their IRBs getting only a few, sporadic proposals to review with meetings being scheduled erratically. In addition to causing delays on decisions of submitted proposals, the lack of regularity caused review work to be regarded non-seriously by researchers as well as IRB members.

Participants also noted occasions in which influential researchers were able to bypass the IRB and approach the institutional head directly for approval of their proposals without going through ethical scrutiny. Others reported pressure being applied by the head of the institution (or any other influential figure of the institution for that matter) on the IRB members for a quick approval of his or her research project proposal by the committee. Since the institutional head is generally a powerful figure, participants felt that it is all the more difficult to resist such directives. A patchy application of ethical scrutiny can result in undermining the credibility of the IRB, with only the junior most researchers being 'trapped' in the review process, and the influential ones sidestepping it effortlessly.

Conference participants also encountered issues particular to multi campus institutions. Some opined that a selective enforcement of the ethical review process of research proposals to only certain campuses undermined the credibility of the IRB and its entire proceedings.

Participants also noted frequent requests for expedited reviews without credible reasons. According to them, this was because researchers viewed the review process as an unnecessary hurdle in the path of research which needed to be crossed. They said that postgraduate students chasing deadlines were the ones making such requests for urgent reviews and issuance of clearance certificates to meet submission deadlines for their theses or dissertations. Such requests were also being directed by research supervisors to the institutional head or the IRB Chair, often one and the same person. The conference participants commented that when questioned, students frequently expressed unawareness of the IRB review requirements.

Requests to Pakistani IRBs for back dated approval was also noted to be a common issue. The researcher having already conducted the research often approached the IRB for an ex post facto 'review' and an approval letter to fulfil requirements for a thesis or paper submission for publication.

Lack of training:

Most of the IRB members in the workshop expressed their concern about their lack of structured training in bioethics. Most of them had on-the-job training as IRB members, and according to the PMRC study quoted above, up to 57% of IRB members in public sector medical institutions and 41% of private sector medical institutions have no formal research ethics training. Participants voiced their concerns about their lack of expertise in dealing with certain protocols, especially those submitted by seasoned researchers.

The concern about training deficiencies is by no means unique to Pakistan and the lack of uniform training of IRB members and the absence of central regulatory processes have been mentioned by others as well.[23]

Conclusions and Recommendations:

The recent increase in numbers of IRBs in Pakistan is laudable. However, an unregulated growth with no central monitoring of these boards is impacting on the quality of oversight provided, thereby damaging the credibility of the process. Interference from institutional hierarchy, COI issues and an inconsistent application of the review process are some of the challenges faced by IRBs in this country.

In order for the review process to be meaningful, institutional leadership has to be sincere in its efforts to constitute independent boards which are allowed to function without hindrance. There is also a need for basic training in research ethics for reviewers, researchers and administrators.

The credibility gap that ethical review currently faces in Pakistan has some valid reasons. The NBC as well as academic institutions have to play their role in infusing integrity into the process.

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