ETHICAL ISSUES OF BIOMEDICAL RESEARCH IN DEVELOPING WORLD AND THEIR SOLUTIONS

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ABSTRACT

Researchers from the developed world usually carry out various biomedical research in developing countries. Citizens of these developing countries are used as research subjects and therefore are exposed to different experiments which risk them to negative effects of the studies while the net benefit is transferred to the developed world. This article highlights the different ethical and moral issues in biomedical research involving the use of human subjects. It will further suggest strategies to make such types of research, ethical and to protect the human rights.

KEY WORDS: Biomedical Research (MeSH), Ethics (MeSH), Bioethical Issues (MeSH).

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INTRODUCTION

In the modern era the development of science and technologies has also brought development in the field of medicine and healthcare. As research plays an important role in every field of life, same is the importance of biomedical research for the advancement and improvement in healthcare. Biomedical research is expanding rapidly, in spite of the potential of having some ethical issues, advancement in health care will remain continue through this research in future.[1] Biomedical research is carried out for the sake of development of new drugs, vaccines, medicine regimen, medical equipment and medical technologies. It also involves the use of human subject like in genetic studies and clinical trials.[2]

Biomedical research is a key for the advancements and improvement in the field of health and medicine, and it has contributed a lot to the promotion of health and improving the qualities of life, in spite of all these benefits biomedical research sometime gives birth to certain ethical issues. Due to socioeconomic disparities between developed and developing countries of the world, the researches on human subjects are mainly conducted in developing countries. Conducting research in developing world is easy and cheaper because of regress ethical regulation, lack of health care resources and poverty and faster speed as compare to being conducted in the developed world. In the third world nations the participant are recruited easily because they are seeking for the fulfillment of their needs like treatment and money etc. becoming human subject in biomedical research make participants prone to exploitation and other ethical issues.

To minimize ethical issues, a number of guidelines for research ethics are developed in the twentieth century and still the ethicist are trying to refine these guidelines. Some of these regulations are the Nuremberg Code (1949)[3], the Declaration of Helsinki (1964, revised 2008)[4], the Belmont report (1979)[5] and the CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subjects (2002)[6] etc. The main focus of the current article is to highlight the main ethical issues related to biomedical research in the developing countries including Pakistan. It will also highlight how clinical research can be made ethical in Pakistan. Some of the ethical issues in biomedical research in developing world including Pakistan are:

The informed consent:

Informed consent is the individual understanding of the facts, its implication and the future consequences of an action and then his or her right to be the part of this act or not (the principle of autonomy) if he or she is competent, and in case of incompetency surrogate decision making, is one of the main issues of research ethic in developing world. This issue was raised when concerns about research ethics in developing countries were pointed out in 1997.[7] The editor of the New England Journal of Medicine pointed out the issue from Tuskegee study[8] in which the poor farmer were not properly informed about the study and they were kept deprived of antibiotics penicillin discovered at that time.

In developing countries like Pakistan there are different issues related to informed consent, like its understanding of language and difficult concepts such as "randomization" or "placebo". Sometime the individual informed consent are difficult to be obtained, instead community informed consent is used for such researches in which the community leaders only have the authority for informed decision making. In some communities male decide for their females despite of their competency for decision making.

Another problem with the informed consent is the incentive attached with it, like the participant think that it is the

only way to get treatment and hence become the part of the study. Sometime the subjects participate in the study for the sake of money or other benefits. The poor and needy people face greater risk because of attached incentive. Incentives undermine a person capacity of free decision making and invalidate the informed consent. According to the World Health Organization's Declaration of Helsinki an informed consent from the human participant is mandatory and the decision that must be made without pressure or coercion.[4]

Standards of care:

The second concern of research ethics in the developing world is the standard of care. The use of placebo control trial in developing countries is another controversy and has been questioned by different organizations.[7] This is a norm in the developed world, that if a therapy or medications for a treatment or prevention of a disease is once decided as standard of care then the use of placebo control becomes unethical in research. The recent revision of declaration of Helsinki states that the use of placebo control should only be allowed if no effective treatment exists.[4] This issue aroused after AIDS Clinical Trials Group (ACTG) conducted a multicenter clinical trial (Protocol 076 - ACTG 076) on efficacy of zidovudine in reducing the risk of maternal-infant transmission of HIV in US and after 1994,[9] ACTG 076 regimens became the standard of care for HIV vertical transmission. However, due to high cost, ACTG 076 regimen was not commonly used in developing countries. Further placebo-controlled trials were conducted in developing countries to search for alternative drug regimen for prevention of perinatal transmission of HIV and patients were unethically deprived of standard antiretroviral drug regimens.[10-12]

Community participation:

An ethical research is one that fulfills the need of community and is based on national priorities, so the research agenda of the developing countries should be grounded in the process of priority setting.[13] Due to low education rate and poverty in the developing countries it is difficult to involve the community in the research questions, its protocol development, informed consent and other matters.

Prior agreements and benefits of research:

According to CIOMS "as a general rule, there should be an advance agreement by the funding agency that the benefits of the study will be made practically available to the citizens of the host community and the country at the end of the successful study. It should be acceptable and approved by all concerned parties before the start of the study".[14] Medical research including clinical trials on particular vulnerable groups are acceptable only if the host community will get benefit from the results of that research.[4,15] Most of the biomedical researches are carried out in developing countries so their citizens are subjected to the risk of exploitation and harm, while its benefits are shifted to the developed countries.[16]

Strategies for making biomedical research ethical

Being a developing country Pakistan is also facing different ethical issues attached with biomedical research. Different research studies are carried out in Pakistan by some local and international research organizations. All the discussed ethical issues exist in Pakistan, in order to resolve these issues and make biomedical research ethical the following ethical steps need to be taken.

1. Ethical guidelines:

Ethical principles mentioned in the World Medical Association Declaration of Helsinki[4] should be followed in conducting biomedical research using human subject. These guidelines are followed in developed world for conducting biomedical researches. It focuses on vulnerable groups of the research study, the informed consent about the study, the use of placebo controls in clinical trials and how the benefits of research might be shared among the researchers and the participants. The vulnerable research participants like kids, mentally retarded and unconscious patients need special protection and also the recognition of their needs.

Those who are unable to refuse informed consent or those who give consent under pressure require special attention. Those who get personal benefit from the research or participate in a research for the sake of treatment also need special attention. The investigator should recruit their participants without any pressure or influence. A clear and well informed consent should be obtained.

The placebo control should not be practiced on new drug if a standard of care is already available in the country. The research should benefit the individuals' subject and the host community.[17]

2. Avoiding human exploitation:

The participant's exploitation should not be avoided in any sort biomedical research. This exploitation may be in the form of unfair benefits or unfair burden of risk for the participants of the study.[18] The causes of exploitation in Pakistan are poverty, illiteracy and ignorance. Furthermore these studies are mainly carried out by the researcher form the developed countries so the lack of sympathy when dealing a local subject might be another problem. The benefit of the research is transferred to the developed world. So there should be an independent review board to prevent human exploitation. To minimize or if possible avoid exploitation the following 8 principle for research ethics with 31 bench marks need to be followed.

Collaborative partnership: Collaboration among the researchers, host community and other related parties is

needed to avoid exploitation.[19] It has six bench marks i.e. partnership among the host community and researchers, assessing the problem and value of the research to the community, mutual respect for the host community's culture, social and political system, minimizing disparities among the researchers, sponsors and the host community, the host community should receive fair benefit of the study, it requires the distribution of tangible and non-tangible rewards among the involved parties.

Social value: The research should have social value; it should generate new knowledge in order to improve health of the population. Without social value a research will lead to human exploitation. It has four benchmarks that are; defining the beneficiaries of the research, then the potential value for each beneficiary will be outlined, the social value to be enhanced and the research will not undermine the existing health care system.

Scientific validity: The research should be scientifically valid with appropriate sampling selection and should be unbiased. The research should be designed which will be advantageous in the context of this area, the study design must realize the objectives of the study and it should be designed according to the social, political and cultural environment of the host community.

Fair subject selection: The subject selection should be fair, unbiased and with a scientific reason for selection of a particular subject and community. To minimize risk, those communities can be selected in which collaboration may be developed and social values can be realized. Different vulnerabilities should be considered. Confidentiality and privacy should be assured and respected.

Favorable risk-benefit ratio: Risk benefit analysis of the study should be performed before starting the study. Studies with greater benefits to risk ratio should be appreciated. And if the potential risk prevails over the benefits of a study then justification by social values is needed.

Independent review: to minimize the researchers' conflict of interest and subject exploitation there should be an independent review board to guarantee accountability. It should work independently without any influence or pressure and should be unbiased.

Informed consent: The informed consent is one of the most important work for making biomedical research ethical, but there are different barriers in developing countries as for as the informed consent is concern. These include understanding of language, cultural values and illiteracy. The host community should participate in establishing the recruitment and incentive procedures for the participants according to their cultural, political and social system. For easy understanding, the Informed consent should be in local language using cultural idioms. It should be acceptable in local community, and it should have the right of withdrawal from the study.

There should be respect for the host community and individual: The participants should be respected in the sense of right to withdraw from the study, respect of confidentiality, should be informed if new information obtained and the benefit of the study should be provided to them.

All these principles of biomedical research ethics with their benchmarks[20] if implemented in Pakistan will help to make research ethical and will help in minimizing human exploitation.

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CONFLICT OF INTEREST

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The sole author **AZ** has made substantial contributions to the manuscript & approved the final version to be published.

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