Brave New World - of Gene Editing: Implications for Pakistan

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"Things are in the saddle, and ride mankind." - Ralph Waldo Emerson

Technological advancements and scientific developments carry a certain allure—technology is useful and at the same time, very seductive. A method that allows you to snip or delete a faulty gene? CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats), one of the tools used for genome editing invented in 2012, is an ingenious discovery in the field of genetic engineering. It holds potential to revolutionize biomedical research, ultimately leading to more scientific discoveries and cures, thereby alleviating patient suffering.

The uses of genome editing are far and wide. Through making specific changes to our DNA, faulty genes that cause diseases such as cancer, neurological and psychiatric issues could potentially be eliminated. The tool has widespread potential for genetic disorders which span across multiple generations.

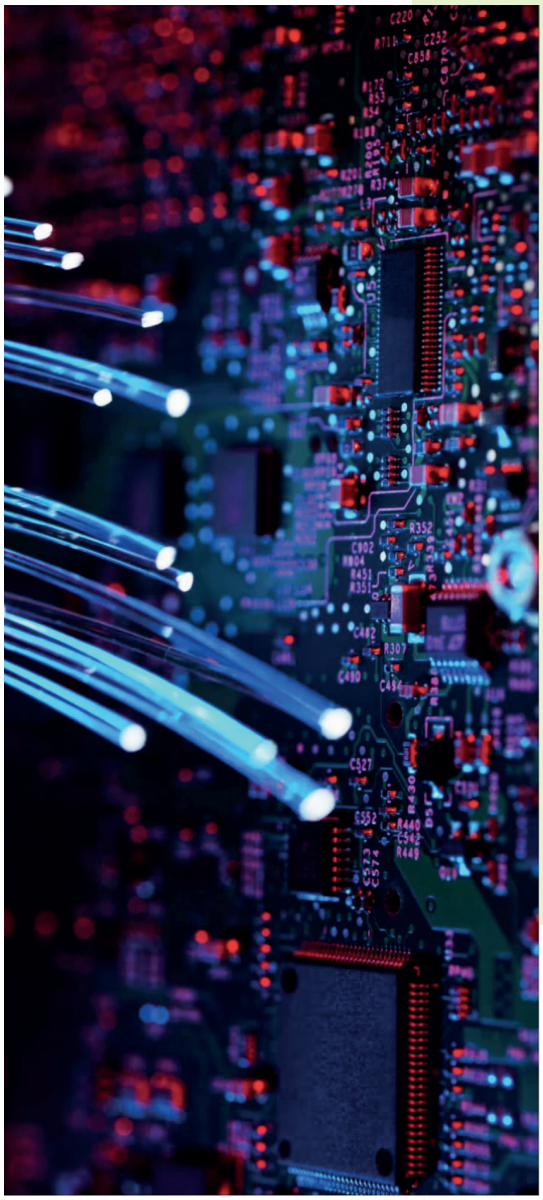
Within the Pakistani landscape, such tools hold a lot of promise. Approximately 16 million of Pakistanis suffer from a rare genetic disorder, mostly among children [1]. One of the most common genetic disorders is thalassemia, considered to place a huge burden on the healthcare system. Every year, 5000 babies are born with this disease with significant impairments in quality of life. At present, the only mode of managing this disease includes blood transfusions or bone marrow transplants, both of which are expensive and extremely debilitating for the concerned individuals, their families as well as the overall healthcare system.

Gene therapies that can potentially delete the gene causing thalassemia and other blood disorders such as sickle-disease anemia are currently being researched upon but they show a huge promise. In Pakistan, the Aga Khan University has recently received a grant to develop a druggable gene editing therapy which will allow the defective gene to be 'sniped' and then repaired for the two

afore-mentioned diseases. While the research is currently located in the laboratory, it will soon move into the real world so that the safety and efficacy of this tool can be tested among humans through clinical trials. Several concerns emerge when new therapies are being investigated among humans, and the waters become murkier within the area of genomics, an area which is not only ill-understood by the general public but also the medical community. The most pressing concern however is that humans who will be part of such studies will comprehend the information being provided to them. This ability to comprehend genetic information is not directly linked to education status—there is reasonable evidence to state that genetic literacy defined "as the capacity to obtain, process, understand and use genomic information in healthcare" is also poor among the most educated [1]. This becomes even more profound within the social milieu of Pakistan where general literacy levels are low. Rates of genetic literacy are unavailable from the country however when studies have been conducted to understand public perceptions towards genetic screening and testing, it has been demonstrated that individuals possess poor knowledge [1]. It should be noted that these studies did not seek to understand perceptions and/or knowledge about genome editing, which is more advanced and carries more technicalities.

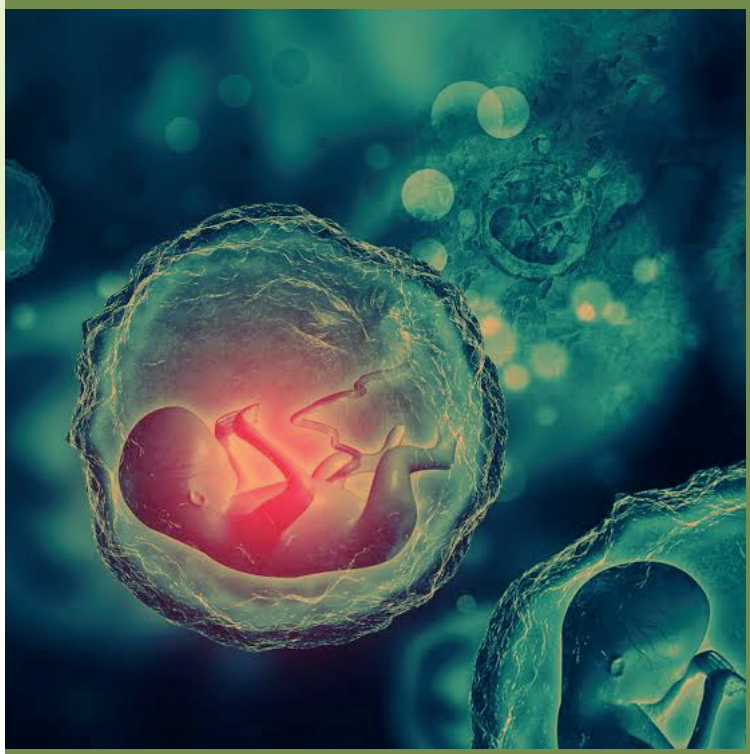
Consider the example of BRCA gene testing and its application in Pakistan. The studies report that not only did patients and their families believe that this test could actually 'cure' the disease, a form of therapeutic misperception that commonly occurs in genomic studies, but they also did not understand the consequences of screening positive for this gene. What clinicians had to offer was a prophylactic double mastectomy and ovariectomy but in the sociocultural context of Pakistan, this can be considered quite inconceivable especially for young, unmarried women. The far-reaching result of this is of course, a loss of trust among the public about scientific advancements, as well as towards the medical community.

Offering the test simply because it is available illustrates not only the lack of foresight of the possible social consequences but also demonstrates that clinicians have not received training throughout their professional careers to provide counseling for genetic-related matters. In fact, in Pakistan, there is paucity of genetic counselors—anecdotal evidence suggests that there are not more than four genetic counselors serving a population of more than 220 million. A parallel can be drawn between genetic screening/testing and genome editing. If genetic screening has been poorly misunderstood over the years in the LMICs context, it can be reasonably assumed that genome editing, the science behind it and its implications for future



generations, may face even greater challenges. This will be exemplified given lack of human resources in this area. A pilot study conducted at Centre of Biomedical Ethics and Culture, SIUT with high school and university students from different fields including medicine in Karachi and Lahore demonstrated limited knowledge regarding the science of genome editing. It was initiated with the rationale that while public perspectives regarding genome editing are available from several high-income countries illustrating varying degrees of knowledge and acceptability towards this technology, voices from the developing world contexts are largely missing.We sought to explore their perceptions of ethical concerns associated with the technology through focus group discussions, a qualitative method of inquiry. Much to our surprise, several participants appeared well informed about the possible ethical issues that may arise. Here I report only the more prominent findings. Since genome editing has the potential to not only replace a faulty gene but also to insert a new gene which can 'enhance' certain traits that individuals are born with, participants appeared to distinguish in their acceptability towards the therapeutic versus enhancement aspect of genome editing. Enhancement was not acceptable whereas therapeutic uses particularly for severe genetic disorders were favored.

But an interesting aspect was that even within the therapeutic arena, participants differentiated in their acceptability. Mental illnesses, for example, became a matter of debate among various participants. Disorders like dementia, with a definite heritable component, that causes immense suffering not only to the individual but also to the family was acceptable. On the other hand, for health conditions such as depression, there was less acceptability for parents deciding to edit the 'depression gene' for their yet unborn child. In the words of one participant, "Anything can happen, accidents happen, they could lose their legs and then they're physically challenged..... You go all this way to make sure that your child never has anything to worry about. How much can you control?"



Mental health experts would of course agree that while several mental health illnesses carry a strong genetic predisposition, the interplay of environmental factors also have a major role. Some would also shy away from viewing depression as a disease but may actually consider it as more of the life view of individuals. Shelagh Stephenson's play (2000), "An Experiment with an Air Pump," set in two different time periods raising questions regarding basic principles of medical research, dramatizes this debate masterfully through a dialogue (captured in the figure) between Kate, a genetic engineer, and her husband, Tom, an English literature teacher.

When Tom states, "... you can't swat it like a fly" it rings eerily similar to sniping a faulty gene with a proverbial CRISPR scissor. Genome editing is a powerful tool but it will be an expensive one. The 2022 patent battles in the United States have reinforced this idea that medical discoveries can be commercialized. This is of course without realizing that medical discoveries would not see the light of the day if human participants had not contributed in the experimentations that made them possible. I return to BRCA. While available in Pakistan, its cost amounts to PKR50,000, making it inaccessible to majority of the population. Findings from our study also show that participants believe that accessibility for the wider population will be a challenge, especially in Pakistan where the majority of healthcare expenditure is out-of-pocket. As a participant voiced, "If you're just privatizing it... that makes it product-like. If I am living in a rural area, and this thing has been privatized, the government doesn't offer it... then I won't get it."

In the backdrop of these challenges, one must proceed with caution before adopting such technological advancements. This is not to state that such technological advancements do not offer solutions to health problems that cause immense misery to individuals. Erik Cassel wrote back in the 1990s: "Technologies come to have a life of their own.... Technology is not the problem; it is the relationship to it of those who employ it that is the problem." The thrust therefore is not to ignore the technology but to contextualize its use to the needs and requirements of the local people. This would mean more engagement with the public, and finding their perspectives about it should be adopted, used, and regulated. Our pilot study was an initial effort to explore what a group of people thinks about genome editing but the limitation was that it included only students from a selected segment of society (English-speaking, upper and middle-income strata). Efforts should be made for greater public engagement and to reduce genetic illiteracy rampant in our parts of the world. Ultimately, it should not be the 'things' in the saddle controlling mankind, as Emerson bemoaned, but rather the reverse.

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