Editorial

The Role of Genomics in Reshaping Healthcare Delivery: Personalized Medicine

In recent years, the practice of medicine has seen an evolution from evidence-based medicine to predictive and precision medicine. The latter differs from the traditional 'one-size-fits-all' approach in that interventions are tailored to individual patients, being customized based on their unique genetic makeup, environment, lifestyle, and other factors.[1,2] This approach has revolutionized how we treat diseases and has empowered patients and healthcare professionals alike, allowing them to make more informed and effective decisions.[3] We can streamline the process of identifying genetic, metabolic, and protein biomarkers by leveraging advanced technologies such as next-generation sequencing, mass spectrometry, and high-throughput content screening.[4]

Personalized medicine has been made possible due to substantial progress in the domains of pharmacogenomics, pharmacometrics, pharmacomicrobiomics, pharmaco-proteomics, metabolomics, big data analytics, and artificial intelligence (AI). Discoveries and developments in these fields have fostered a deeper understanding of diseases at a molecular level and helped identify how the pathogenesis of a disease may differ between individuals. This has in turn enabled the development of innovative treatments that were once considered unattainable. Further, the advent of personalized medicine has paved the way for better-targeted therapies, that are associated with enhanced treatment efficacy while minimizing adverse effects.[5] As a result, patients are experiencing improved outcomes and a better quality of life.[6]

Oncology

Personalized medicine relies on the ability to leverage vast amounts of biological data, such as genomic sequences and various biomarkers in a large group of patients to identify how a person's genetic code influences their response to various treatments.[7] The study of genomics has contributed to major advancements in oncology, such as the development of targeted therapies that are used to treat patients with tumours containing specific genetic mutations that drive cancer, such as HER2-positive breast cancer or epidermal growth factor receptor (EGFR)-mutated non-small cell lung cancer. Other important examples include the identification of homologous recombination pathway deficiency and the use of poly ADP ribose polymerase (PARP) inhibitors in treating certain ovarian and breast cancers.

The personalized medicine approach has also permitted the use of interventions such as checkpoint inhibitors and personalized vaccines, which enhance the body's immune system to specifically target cancer cells without injuring the surrounding healthy tissues.[8] Further, it has permitted modification of the dose of fluoropyrimidine in persons identified to have variations in the dihydropyrimidine dehydrogenase (*DPYD*) gene, thereby reducing the risk of drug toxicity; similarly, testing for *TPMT* or *NUDT15* genetic variants can help prevent toxicity due to 6-mercaptopurine therapy.[6]

Other domains

Besides oncology, other fields of medicine have also benefitted from the personalized approach. In cardiology, pharmacogenetic testing helps identify individuals at higher risk of adverse drug reactions to antiplatelet drugs or statins,[6] enabling early institution of preventive interventions, such as dose modification or administration of an alternate medication. In some inherited 'rare diseases', personalized medicine

offers targeted treatments that were once unimaginable, such as anti-PCSK9 (proportain convertase subtilisin/kexin type 9) antibodies for the treatment of dyslipidaemia.[7]

Another personalized medicine approach is through the use of antisense oligonucleotides that selectively target mutations at the RNA level. These have been shown to be efficacious in conditions such as spinal muscular atrophy, dyslipidaemia, and hyperoxaluria.[9] RNAi therapies targeting *ANGPTL3* have also been shown to be beneficial in dyslipidaemia, being as good or even better than the antisense oligonucleotide therapy.[10] Genomic technologies have also contributed to the development of these interventions by shedding light on genetic variations that alter the function of specific key players in the biology of some specific diseases.

Therapeutic drug monitoring and a combination of such monitoring with pharmacogenomics aid dose optimization of drugs; this has been shown to be associated with improved treatment outcomes, especially in psychiatry[11] and infectious diseases.

Impact of AI

Advances in technology that allow data acquisition in real time through mobile platforms have provided tools to aid in patient stratification. Digital health technologies, such as wearable devices allow continuous monitoring of biomarkers, such as glucose levels, heart rate, and blood pressure. The analysis of these complex datasets and the data on genetic and protein markers are quite massive and thus need analysis using AI tools, such as machine learning which allows detection of patterns and make treatment recommendations in real time.[12]

Integrating AI in personalized medicine offers unprecedented opportunities. For instance, integrating AI into genomic datasets can help identify the association of specific genomic variations with drug responses, and thus help in predicting outcomes in individual patients, as well as designing personalized treatment plans tailored to each patient's unique genetic profile.[12] Thus, AI can help improve patient outcomes and reduce healthcare costs.

India has recently announced its intention to create a database of 10 000 human genomes, representing 83 population groups—approximately 2% of the 4600 population groups (*https://ibdc.dbtindia.gov.in/*). The Genome India database will serve as a resource for research to understand population-specific pharmacogenetic variants, disease mechanisms and enable decisions for personalizing drug therapies (*https://genomeindia.in/*).

Challenges and future directions

While personalized medicine holds immense promise, its implementation poses major ethical, social, and economic challenges.[13] In particular, it needs the, setting up of adequate, suitable and sustainable infrastructure and skills among medical professionals. The latter need to move away from the traditional methods of diagnosis and treatment, and to join hands with professionals from other fields to build teams of personalized medicine practitioners. For instance, pathologists who have traditionally been looking after genetic testing and reporting need to work together with molecular biology experts and clinicians, forming specialized teams, e.g. molecular oncology, molecular cardiology, etc. Development of such interoperable and shared resources will be key to the sustenance of the practice of personalized medicine.

While genetic sequencing and tailored therapies are increasingly becoming available, their cost remains prohibitive for many patients, particularly in resource-limited settings, including India. Therefore, studies evaluating the benefits and cost-effectiveness of such approaches, especially in low-income settings, are urgently needed.

The complexity of genetic testing and interpretation poses a barrier to its widespread use. However, advancements in AI can streamline these processes by aiding quick interpretation of these data, thus reducing costs and making personalized medicine more accessible. However, the integration of AI into personalized medicine raises important ethical considerations, including those related to data privacy and security. Collection of sensitive genetic information at a large scale carries the risk of data breach and misuse. Transparent policies for data collection, use, and sharing are essential to prevent such misuse and to build trust between healthcare providers and patients.

Importantly, simple measures such as lifestyle modifications, patient education, and efficient communication should not be overlooked while promoting personalized medicine, since the former are not only cheaper and simpler, these add to the probability of optimizing therapeutic outcomes and minimizing adverse events.

Finally, it is essential that all healthcare providers receive continued education in the domain of personalized medicine, to ensure their readiness to embrace these scientific and technological advances and implement these in their clinical practice.

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