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HEALTHCARE TRANSFORMATION THROUGH PERSONALIZED MEDICINE

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ABSTRACT: Excessive heterogeneity in the phenotypic expression of drug treatment response and adverse drug reaction is resolute by a complex interaction of multiple hereditary variants and environmental aspects. The complex nature of treatment response greatly increases the need for personalized medicine. Drug metabolizing enzymes show monogenic genetic polymorphism and influence drug response. Cytochrome P450 enzymes have clinically relevant variation in their effects. Understanding the genome, proteome, plus metabolic pathways have improved drug development. The application of pharmacogenomics, the use of biomarkers, the molecular system approach, and metabolomics technology will certainly help in the development of personalized medicine. Proteomic technology requires further development for analyzing a massive amount of genes and protein profile data. There is the need to cheer a paradigm shift from traditional medical practices to personalized medicine. Due to the high prevalence of inherited genetic disorders and non-communicable diseases, personalized medicine has its own significance. It aims to enhance awareness, motivation, and sincere efforts towards better and cost-effectiveness.

INTRODUCTION: In the existing traditional healthcare system, substantial inter-individual variability can take place in the clinical response to drug management for acute as well as chronic illnesses. Around 50% of patients respond to their medication, remaining either not receiving the proper medication, suffer substantial therapeutic delays by substituting from one medication to another resulting in adversarial drug reactions, or having fatal ADRs in 0.32% cases [1, 2]. Excessive heterogeneity in the phenotypic manifestation of the drug treatment response and ADRs is definite by a multifarious interplay of numerous genetic variants and environmental factors [3, 4].

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The complex nature of treatment reactions significantly raises the need for personalized prescriptions. Personalized medicine (PM) is definite as the distribution of the right drug to the right patient at the right dosage and is consequential to the application for pharmacogenomics into clinical practice [5]. Future advances in genomics, diagnosis approaches, data analysis, clinical decision-making, and sustainable business model for personalization of therapy can speed up the individualization of therapy based on genetic makeup [6]. Pharmacogenomic and pharmacogenetic testing, which identify genetic variants that can help predict drug efficacy and/or toxicity, are important contributors to the field of personalized medicine. Interactive genomics in conjunction with environmental, social as well as lifestyle factors will become vital to recognize the predictive, preventive, personalized as well as participatory medicine (PM) as the future paradigm of the healthcare system [7].

Healthcare distribution schemes come across new challenges as they acclimatize the fresh requirements in addition to practices related to personalized medicine. They recognized five overall areas of challenges, *i.e*., patient empowerment, value recognition, education and awareness, safeguarding access to care, infra-structure as well as data management. PM offers better therapeutic response and lesser adverse drug reactions.

Ultimately, it reduces the healthcare cost burden among the society, particularly in cancer, cardiovascular diseases, psychiatric disorders, and hemoglobinopathies. There is a need for the insertion of pharmacogenomics in addition to personalized medicine into the community healthcare system. Recent advances in diagnostic medical imaging and molecular medicine are gradually transforming healthcare services [8].

Need of Healthcare Transformation through Personalized Medicine:

Five significant categories affecting the evolution of personalized medicine are as follows [9]:

1. PM aims to shift medicine value from reaction to prevention, giving the selection of the most favorable drug treatment and less trials, making the safer drug use by reducing side effects, reducing the time and cost of trials, reducing the healthcare cost, enhancing patient compliance with health treatment.

2. Personalized medicine includes faster growth like new implement to convert the human genomes more precisely, an extensive study that helps to link genetic variation to disease, and information technology regarding health that secure the combination of research and clinical data.

3. Investigation of genomics and the effect over personalized medicine.

4. Details about legislation and groundbreaking policy.

5. Hospitals, regional healthcare systems as well as educational organizations endorsing clinical assumption of personalized medicine through clinical research and medical education betterment. Therefore, the targeted therapies and targeted dosing based on genomics, personalized medicine can be observed further, broadly as an inclusive, prospective approach to inhibiting, detecting, treating, plus checking disease in customs that achieve optimum individual healthcare decisions [10].

Role of Pharmacogenetics in Personalized Medicine: Personalized medicine has the ultimate goal of matching each therapeutic intervention with the patient's molecular profile [11]. Therapeutic response varies from one patient to another, and few patients show adverse drug reactions at same therapeutic dose [12]. It is the study of different responses to medications due to genetic variations in individuals. Innumerable genes could play a role in toxicity and drug response. Genes are DNA segments that are found in all cells of humans, and they are able to affect a person's response to medications. A gene may have numerous different chemical messengers and forms that affect drug activity in the body [13].

TABLE 1: DRUG METABOLIZING ENZYME

Drug Metabolizing Enzyme	Name of Drugs	Effect of Polymorphism
Cytochrome P-450 2D6	Nortriptyline	Improved drug effect
Cytochrome P-450 2C9	Warfarin,phenytoin, Losartan	Improved drug effect[17]
Cytochrome P-450 2C19	Omeprazole	Improved drug effect
N-Acetytransferase 2	Isoniazid, Hydralazine	Improved drug effect[18]
Catechol O-methytransferase	Levodopa	Improved drug effect[19]
Drug Metabolizing enzyme	**Name of Drugs**	**Drug Toxicity**
Thiopurine s-methytransferase	Azathioprine, Mercaptopurine	Increases drug toxicity[20]
Dihydropyrimidine dehydrogenase	5-flurororacil (5-FU)	Increases drug toxicity[20]

Examples of genetically polymorphic and toxicity in phase 1 and 2 enzymes showing variations clinically in their effect

All phase of pharmacokinetics that is absorption, distribution, metabolism also excretion potentially involve clinically significant genetic variations. Few patients with very great or very little plasma or urinary medicine concentration show biochemical characters leading to this variant of genetic

inheritance. Medicine metabolizing enzyme identified shows monogenic involving single genes due to genetic polymorphisms. Passageways of drug breakdown as one or the other phase 1 reaction including oxidation, reduction, and hydrolysis or else phase 2 conjugation responses containing acetylation, glucuronidation, sulfation as well as methylation all may be affected by genetic variations. The cytochrome P-450 enzymes, a superfamily of microsomal drug digesting enzymes, has clinically relevant variations in their effects [14, 15, 16].

Applications of Pharmacogenomics in Personalized Medicine: The field of personalized medicine uses genomic approaches to tailor therapeutics, prevents disease, and promotes health. Pharmacogenomics is the study of genome, which deals with the particular person's drug response based on the genetic. Revealing the illness phenotype distinguishes by a clear genetic outline which may assist to focal point successful treatment on little patient subpopulations.

Within next coming years, it has the potential to offer many benefits like enhanced drug selection, safer dosing options and upgrading in drug advancement.

Genomic, proteomic, and metabolic pathways awareness have grown in current years, leading to the greater advancement in the population of database investigation methods and reducing expenditure on healthcare by shortening the clinical trials and aims for better patient therapeutic response patients safety outcome.

With the discovery of the human genome project, future application of pharmacogenomics in the pharmaceuticals pipeline is introduced in phase 2A and phase 2B of clinical trials, with the goal of the development of new molecules that reduce related risk and cost. Pharmacogenomic tests based on the genotype of an individual can be considered biomarkers. These biomarkers have been planned as powerful implements in animal and human studies in clinical trials and ultimately in clinical practice.

Healthcare organizations have started to embrace the extraction of information from digitalized clinical records and imaging data [21, 22, 23].

Applications of Pharmacogenomics in Clinical Practices:

- Cancer therapeutics Trastuzumab a monoclonal antibody obstructing HER2 receptors, Erlotinib and Gefitinib are tyrosine kinase inhibitors used in cancer therapy[24].
- Cardiovascular diseases- variation in dose-response is due to decrease CYP2C9 enzymatic activity. Effect of Clopidogrel is widely used in the treatment of coronary artery disease and myocardial infarction. The response of clopidogrel was determined by the enzyme CYP2C19 genotype. This has resulted in a marked decrease in platelets responsiveness [25, 26].
- Psychiatric disorders Typical antipsychotics show action on the dopamine pathway have significant polymorphism with dopamine receptors DNA segment DRD2 and DRD3 and response result. Atypical antipsychotics agent serotonin has an association with serotonin receptors gene HTR2A and HTR2C[30].

Application of Metabolomics in Personalized Medicine: Metabolomicsis a key tool for biomarker discovery and personalized medicine and has great potential to elucidate the ultimate product of the genomic processes. Metabolomics incorporates the maximum progressive approach to molecular phenotype classification. It makes the ideal technology platform for the sighting biomarker pattern as well as the disease state for the personalized health monitoring program and for the design of individualized interventions [31]. Use of system molecular biomarker profile as avital tool for enhancing the drug discovery and drug development process and for an improved molecular understanding of diseases process, drug safety and drug efficacy to identify treatment responders/ non-responders in clinical trials. The advantages of metabolomics are to reduce advancement time, minor focused clinical trials, and improved safety attractive profitability [32]. A molecular system methodology and the application of metabolomics technology will definitely play in the development of personalized medicine [33]. Metabolomics is definite as the comprehensive, quantitative, and qualitative analysis of altogether small molecules in a system.

The coverage certainly has improved in metabolomics research over the past decade [34, 35]. The use of metabolomics has proved clinical significance in the treatment of diabetic nephropathy and rheumatoid arthritis [36, 37].

Status of Metabolomics in Personalized Medicine: Modern metabolomics strategies are composed of various methods such as:

- Nuclear magnetic resonance (NMR) [38].
- Gas chromatography-Mass spectroscopy (GC-MS) [39].
- Liquid chromatography-Mass spectroscopy (LCMS).

Mass spectrometry is mainly essential to expose metabolites pattern at low concentration; for example, urinary metabolites are detected in Paracetamol poisoning. In schizophrenia, a study that engaged lipid engrossed metabolomics associated with the effects of olanzapine, risperidone to a phenotype outline.[40]

Advantages of Personalized Medicine in Pharmaceutical Industry: Assisted marker recognition use and selected remedy gained from a particular person molecular study will definitely influence the system drugs are developed [41]. The novel target recognition, toxic genomic indicators to screen compounds, and choice of clinical trials patients can be achieved by an understanding of the molecular diagnosis that will transform the pharmaceutical industry and will replace the conventional test and medicine error. To forecast the risk of evolving diseases molecular indications, the usage of DNA or messenger RNA from the biological marker is done.

The early stage of finding counting selection and acceptance of drug site, fine molecule screening, chemistry, and before clinical evaluation of compound is linked with the later stage of clinical evolution [42]. Identification of cell surface protein, the secreted protein might be utilized as a record marker in medicine evolution [43, 44]. Toxic genomic highlighter foretelling of unfortunate medicine response might impact choosing and expansion of leading mixture ahead human researches for hepatotoxicity, nephrotoxicity, cardiotoxicity, or bone marrow suppression [45]. These studies are conducted for patient welfare in drug evolution.

Clinical tests are now conducted by the educational, medical center, and clinical examination institute for drug ability and welfare in the process of medicine outcome [46]. New treatment strategies may be progressed nearby the non-responders in a particular molecular subclass of diseases.

Use of Personalized Medicine will give following Advantages to Pharmaceuticals Industry:

- Increase efficiency and reduce cost.
- Reduce the time and cost of evaluation tests.
- Arrival of an advanced gene selected for medicine find.
- Drug distinction in the trade.

Advantages of Personalized Medicine in Patient Care: The eventual aim of personalized medicine is to outline disease at the molecular level so that the defensive resources also the therapeutic agents can be fixed at the right population of people though they are still healthy.

Individuals deemed at high risk of disease can be targeted for preventive therapy and lifestyle modification. The submission of innovative technologies, as well as the integration of data from an individual, will lead to a new paradigm in patient care. The base of genotype-focused treatment will be the genetic variants associated with increased or decreased threat of disease.

Examples:

- Prevention of myocardial infarction and stroke as well as hypertensive patients [47, 48].
- Measurement of mammogram or blood pressure and Pap smear will explain further exactly the prediction for growth of diseases in cervical carcinoma, breast carcinoma and in renal failure [49, 50].
- Different molecular markers can determine a destructive form and quick progression of diseases in diabetic nephropathy, diabetic retinopathy, and diabetic neuropathy.

Use of Personalized Medicine will give following Advantages to Patient and Clinicians:

- ❖ Greater possibility of anticipated outcome with a drug.
- ❖ Little possibility of untoward side effects.
- ❖ Defensive strategies.
- ❖ Intensive therapies.
- ❖ Reduced cost of the drug.
- ❖ Better health and healthcare.

Confrontation with Personalized Medicine: 21th century, there is innumerable summons in discerning the personalized medicine perception. To disclose DNA variants that forecast common-complex diseases that result from a grouping of gene and environmental factors will necessitate budget effective, high throughput genotyping, huge well-characterized patient populations, sophisti-cated computational methodologies, and a complete considerate of the biological path of disease [51].

Revealing messenger RNA as well as protein markers for usage in screening, analysis, prognosis, and observing of the disease will have its own challenges. Examining a massive amount of gene also protein profile data is important for proteomic technology development. Genotyping, in addition to molecular characterization mechanization along with conventional clinical statistics group should be included in medical examination and should accept a repository of victim specimen. Suitable patient controlling organization, academic implement, genetic advised, and non-segregated databases are not in place [52].

The Following Challenges Personalized Medicine is facing in today's Scenario:

1. **Uncovering Protein and mRNA Marker**

- Less expert people are available for sample detection.
- Proteomics study is not developed.

2. **DNA-based Marker Finding or Single Nucleotide Polymorphism**

- Large patient population
- Costly genetic test
- Not as much computers are available for maintaining records.

3. **Practice Marker usage**

- Social, ethical and legal inspection.
- Healthcare awareness is less.
- Understanding and management of the data.

Need for Healthcare Transformation and its Advantages: The sincere efforts for healthcare transformation will definitely mark the evolution on the way to a personalized medicine [53]. Strategies, as well as clinical support highlight over the finest care for individual patients, can be repeatedly restructured to embrace personalized medicine concepts besides practices. By means of latest technologies of high value for PM amenities also biomarkers examination are suitable for together medical practitioner and patients [54]. The researches agendas that do take place characteristically translational research will surely be valuable to a specific patient population plus type of healthcare institutions to be evaluated considering the strategies and recommendations for healthcare transformations [55]. There is the necessity for the evolution of strategic programs as well as efforts to boost a paradigm shift from traditional medical practices to personalized medicines.

Certain Strategies for Transition of Traditional Medical Practice to Personalized Medicines are as follows: [56]

1. **Education and Awareness:** Healthcare providers, patients, employers, and policymakers want to have a healthier understanding of PM technologies and concepts [57].

2. **Patient Authorization:** Guidelines besides practices related to patient engagements, confidentiality, data securities, and other moral, legal, as well as societal concerns regarding the use of individual molecular info must guarantee proper consent also be suitable to patients [58, 59].

3. **Value Acknowledgement:** Finest practices must be established for the collection and dissemination of evidence needed to demonstrate the clinical utility of personalized medicine and ensure the recognition of its value to care.

4. **Substructure and Data Management**: Effective healthcare delivery infrastructure and data management systems need to be developed and applied so that individual patients and clinical support data is comprehensive, useful, and user-friendly, and so that it can be used to guide clinical decisions [60].

5. **Admission of Right Care:** Greatest practices to be carried out for healthcare distribution methodologies, process and program operations that ensure access to personalized medicine must be established and implemented.

Personalized Medicine Role in Transformation of Healthcare Society: Personalized medicine refers to as the Predictive, preventive, personalized, and participatory medicine system. For the emerging transformation of healthcare, it is the practical vision [61, 62, 63]. Personalized medicine is today predominantly a matter of innovation policy; it is primary defined in terms of economy and commerce. Personal information is demanded by the networked consumers, which can use for the improvement of their health [64]. P4 medicine will provide disease care; it will play a role in reducing the disease incidences and will help in replication the innovation cycle of medicine system [65]. System biology and system medicine are exploring the new understanding of P4 healthcare system. System biology refers to the science of the system related to biological functions. It is termed as network collection at many stages ranging from the molecular level from organisms to genes [66]. System medicine is the biology system implementation to diseases occurring in humans. It treats biological systems as ensembles of networks at molecular level [67]. System biology and system medicine have an equal approach towards the challenges of human complications in a comprehensive understanding of person biogeography. The hereditary build-up can be interpreted by the data analysis and information about the surrounding healthcare and illness. It will help in the prevention, early diagnosis, and better management of various diseases like Breast cancer [68], prostate cancer [69], diabetes, Parkinsonism, autoimmune diseases, and psychiatric disorders. Secondly, the drug evolution by following methods can be more powerful because they are selected to exact the lamination of the sufferer. For medical-based industries, this medicine will be cheaper in growing specific patient drugs for the specific patient. PM can fulfill the requirement to improve health outcomes by reducing healthcare costs, drug-development costs, and time [70].

Ways of Transformation of Healthcare Systems for the Mankind and Healthcare Zone:

- Biomedical adaption promotes data points for a particular person in the population and extensive data analysis [71].
- From symptoms to causes, the molecular and cellular origin illness is identified also treated along with cost efficacy [72].
- Biomedical revolution is appearing as uncovering of causes of various disease and their treatments [74].
- Healthcare based on science is expanding the delivery that is moving from clinic to workplace of patients [75].
- In the 21stcentury, the new welfare of industry is rising to appear that will become a vital origin of economic magnification in the next 10-15 years.

Future perspective of healthcare transformation will bring further progress in all five transformations discussed above.

CONCLUSION AND FUTURE PERSPECTIVE: Personalized medicine is a crucial constituent of recent health care practice. It has the probable to modify therapy with the finest response besides maximum safety edge to make sure improved patient care. The worldwide usage of drugs in the 21st century has exposed significant in addition to documented individual differences in therapeutic response. The knowledge of genetic bases of the response to psychiatric medication and the beginning of their side effects has significantly amplified in the last decade. Genetic variance in genes and coding for pharmacokinetic elements involved in the metabolizing process of drugs revealed to forecast, to some extent, change fundamental goals of clinicians to adopt available medical tests and technologies to discrete patients.

In the future as pharmacogenetic testing becomes widely available, personalized medicine will make usage of genetic data in order to dissect the complex picture of inconsistency in response to treatment and expression of ADRs.

The pharmacogenomics approach in cancer is already implemented in clinical practice. Analytical and drug research currently seek out genomic and molecular level directing of cells, tissues, plus organs. Sub molecular mechanism underlying projected therapeutic and unplanned ADRs that may grasp the prospective to optimize or in some cases, revolutionized medical therapeutic education, economics, and ethical encounters needs to be encountered in the putting into practice process of pharmacogenomics as well as personalized medicine healthcare system. Metabolomics is the diagnostic platform that is at present accomplished of unfolding the phenotype most comprehensively. Biomarkers as healthiness pointers are instantly needed to move the personalized medicine field forward.

There are numerous prospects besides challenges to the future of medicine and healthcare for recognition of P4 medicine; there is a clear insistence to organize healthcare systems and policymakers in a particular interval. As the healthcare system mark the transition from its traditional one size fits all methodologies towards a personalized medicine paradigm, it will be essential to over challenges in numerous areas. Some programs and policies such as those allied to education, alertness as well as patient's empowerment can be applied.

At present several healthcare distribution societies are vigorously involved in instigating personalized medicine plans throughout the world. In the future, there is the necessity of setting up suitable leadership also forums to scheme and recruit programs and guidelines that will drive value credit and effective organization and data management system.

By instigating these approaches, we can position healthcare carriage organizations to address challenges related to acclimatizing treatment methodologies and, finally, the process that will confirm access to personalized medicine and thereby endure to use in a new era of medicine.

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