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Research Article

**PERSONALIZED MEDICINE—A MODERN APPROACH FOR  
THE DIAGNOSIS AND MANAGEMENT OF HYPERTENSION**<sup>1</sup>Dr Jawaria Nafees,<sup>2</sup>Dr Khurram Shahzad,<sup>3</sup>Dr Waqas Ahmed.<sup>1</sup>WMO, DHQ Hospital Hafizabad.<sup>2,3</sup>MBBS, Nawaz Sharif Medical College, Gujrat.

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**Abstract:**

Since many years ago, a reduction in blood pressure is used to treat hypertension associated with the physiological state and to overcome the menace of cardiovascular disease. Despite the effectiveness of antihypertensive drugs and lowering the main risk factors, the preventive measures to attain the control of blood pressure is still awful because of the number of factors counting, apparent drug resistance, age, gender, physical activity, and non-compliance to medications. The analytical thinking elucidation about issues related to hypertension management approach is taking light to the complexity of the disorder and lack of adherence according to the required diversity of the pathophysiology and disease presented clinically. However, certain risk elements such as genetics, the study of drugs affect on the body, and various other characteristics differ from patient to patient, were very helpful in the management of personalized approach of the disorder. Personalized medicine has become a subsequent paradigm for health-care as it tailored the medical approach and treatment of each patient with specific individual features. The rapid alteration of the biology research system with the advancement of new technologies and the contribution of different omic characterizations have shifted the traditional way of data design to the data-driven system to speed up and facilitate the adaptation of personalized medicine for hypertension.

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**INTRODUCTION:**

Hypertension is the leading cause of disability, death,<sup>1</sup> an approximate 9.4 million deaths every year,<sup>3</sup> and more than one billion people are affected, prevalence affects around 40% of the general population, 7% in younger age 18-39 -year-old and 65% of age group 59-year-old.<sup>2</sup> Hypertension has increased total global disease burden such as more than 3.5 times that of cardiovascular disease as compared to smoking while 1.6 times that of hypercholesterolemia.<sup>4</sup> A cohort studied reported that linear association was found between the blood pressure and vascular disorder with started 115/75 mmHg without threshold.<sup>5</sup> As the increasing population in terms of size, age, and obesity would proliferation hypertension, with complications of targeted organs correlated to arteriosclerotic. Similar associations were observed in large groups of populations that may be with or without vascular disease.<sup>6</sup> Remodeling processes of tissue and organs has persuaded by hypertension may affect the anatomy of the heart, arteries, kidneys, and brain. Targeted organ complications present the multiple abnormalities such as diastolic and systolic malfunctions, congestive heart failure was recorded in 39% men and 59% in women, coronary disease, stroke, nephrosclerosis, and renal failure. If blood pressure remains as without treated it may cause organ damage in 50% hypertensive people. Although, hypertension is the most prominent risk factor to develop cardiovascular disease.<sup>7</sup>

Despite the availability of hypertensive drugs and efficacious hypertensive therapies, greater acknowledgment of people about preventive measures of hypertension complications and their reduction factors are still not enough to control the blood pressure. Data obtained from a study Italian population where 60% of patients were under observation for hypertension treatment and only 33% of patients has secured to maintain the control of blood pressure.<sup>8</sup> On the other hand, patient's dissatisfaction with therapy, in clinical practice produced a trial and error leads them to switch another medication after a few weeks of the chosen therapy. Similarly, in case of poor adherence considerably, variation has noticed including individual response to treatment, individual characterizations, and drug adverse effects, commonly these are not harmful to patients but may make them frustrated which evenly becomes the reason to disconnect the therapy.<sup>9</sup> The obtained information is derived through the random clinical trials and it can be used for particular patients.

Moreover, a patient under consideration of reductionist during the clinical trial that supposed the common phenotype and treat them accordingly, data derived from large populations research while results did not distinguish the sub-type of the individual. This approach known to one size fits all which is not presently used by biomedical research to clear the differentiation among the disease presented.<sup>10</sup> A personalized approach brings a better improvement in disease diagnosis and risk determination based on disease pathology, symptoms, and patient's satisfaction with treatment. It explored the new strategies to identify the pathophysiology, ameliorate the therapy by adapting the pathway to achieve the adequate adherence, and as well as levels of blood pressure and organ damaged would be different among the different patients, because of environmental factors and development of variation at genome level.<sup>11</sup>

**A Framework for Understanding Personalized Treatment of Hypertension**

Generally, personalized treatment strategy evenly based on the information about the individual in clinical decision making. Mostly personalized strategies for treatment are more value able for patients where strategies with less information are observed to less effective while with the extent of complexity it can be worthy for clinicians. Few awful information-based treatment strategies including the non-pharmacological procedure to control hypertension with changes the mode of lifestyle and recreation are proven fruitful for some people.<sup>16</sup>

In the case of resistant hypertension, synchronous use of three classes of antihypertensive drugs to make good adherence is an instance of bad management of medication which can create more trouble to current issues, risks, and vexation. As a result of the comparison, resistant hypertensive patients are at greater risk of unpropitious effects than on non-resistant hypertension.<sup>17</sup> A drug class, mineralocorticoid receptor antagonists with pathophysiology potently recommended to the patient of resistant hypertension caused by primary aldosteronism. However, it is effective for resistant hypertension treatment but mineralocorticoid receptor activation can not be used for all the resistant hypertension cases.<sup>18</sup>

**Table. 1: Rational process logical follow up**

<b>Diagnosis</b>	Presenting symptoms, examination, and investigation of past medical, and drugs history
<b>Treatment</b>	Considered patient wishes, expectations, values, prognosis, and goals of therapy including the cure, symptoms control, prevention, and quality of life.
<b>Prescription</b>	It includes the drugs, dose, route, frequency, duration, and also considered the patient factors (age, sex, interacting disease, interactive drugs, and genetics), and drug factors (pharmacokinetics, pharmacodynamics, evidence base, cost-effectiveness).
<b>Patient counseling and follow up</b>	Patient complete counseling, and monitoring the effect and follow up.

#### Personalized approach to hypertension

Personalized therapy in hypertension states the condition of particular groups of traits which create the distinction in the response of each individual patients. In order to gain better identification in personalized management of disease, the distinctive molecular profile of individual patients should take into account in a modern approach along with the diagnostic and screening procedure. Pathophysiology of hypertension has an interaction effect of few factors that are gene susceptibility, physiological and environmental factors, which gradually changes with the passage of time.<sup>15</sup>

#### Stratifying patients based on renin profiling

From many decades plasma renin activity (PRA) has been explored in blood pressure regulation and also in response to drugs that stratify with regards to renin, sodium, and profile volume. Initially use of renin profile guidance has achieved characterized treatment to maintain the blood pressure in the control condition in comparison with the clinical decision and precision medicine for hypertension laid the foundation on the base of representation of phenotype physiology. The reduction of effectiveness of this approach is due to a few questioned for clinical utilization of renin profile such as sex, race, analysis issues, and previously taken drug treatment.<sup>12</sup> The plasma renin plays an important role in the determination of the patient's sensitivity to salt by measuring circulating plasma renin as its low quantity provided the Na<sup>+</sup> excess marker. This diagnosis the therapeutic choice for diuretics especially, native Africans are more reactive to diuretics, who are suffering from salt-sensitive hypertension. Therefore, the ethnicity of individuals assist to stratify treatment.<sup>13</sup>

#### Personalized 'omics' in precision medicine

In personalized medicine, omics studies assisted relevant to individualized perspective characterization and information about the hypertension subgroups. The precision medicine foundation constitutes may include the proteomics, transcriptomics as well as metabolomics which

define the fingerprinting and markers. These profiles help in the indication of phenotype which allows monitoring the physical state of the patient with more details.<sup>14</sup>

#### Epigenomics study

Epigenomics is associated with the study of the genome and provides complete information about the modification in genetic material which is captured because of environmental, and lifestyle factors then analyzed and quantify at the molecular level is also known as the epigenome. Thus, causing several complex pathological complications, including hypertension, cardiovascular disease and enhance the mortality rate.<sup>19</sup>

Genome-wide association reported about the research on hypertension and come across 63 loci has an influence on blood pressure, which is also responsive for variation less than 1% in the population. According to the Framingham Heart Study population, identified the variants in hypertension patients, the phenotype of severe hypertension, and also those prevent hypertension.<sup>20</sup> Among these variants, some can be used to target therapy for individuals. Each individual has its specific genome, and lifestyle therefore, it's completely understood that the same drugs may show different responses to disorders. Thus, inter-individual variations and insufficiency to drug response may because of genetic polymorphism.<sup>21</sup>

The recent advancement in epigenomics has developed new strategies for specific groups of hypertension patients who may get beneficial treatment from particular therapies. For example, aldosterone targeted modified sodium channels epithelial 1  $\alpha$  subunits which has been clarified to present hypermethylation of histone H3 at lysine 79 at subpart of the promotor in a few patients.<sup>22</sup> The effort to make in the identification of functional genetics and epigenetic markers is eminently vital to generate a method based on a genetic biomarker

that can work as assistance in managing hypertension from an individual point of view.<sup>23</sup>

#### Future of personalized medicines

Now the therapeutics are becoming the part of this new era of precision medicine where therapy will be individualized based, taking in account the drugs handling according to genetic variants and action, enable to create findings of specific prediction.<sup>24</sup> so, in future of personalized medicine of hypertension, there will be more attention on variables which can alter with time rather than focusing on DNA sequences. The data which may be very helpful for hypertension treatment produced through the combination of multiple fields like, epigenomics, metabolomics, proteomics, and transcriptomics. The obtained data aids in the determination of genetic susceptibility, and also monitor the physical state of the patient.

Moreover, this approach provides an opportunity for the patients to participate actively as a central participant of the complicated network. To realize the huge potential of personalized medicine, for individual patients and to achieve the ultimate goal for a large population, proper knowledge and training for health care providers should be necessary.

#### RESULTS

The data obtained from the analysis of the pathophysiology of hypertension for personalized medicine, 340,000 individuals have identified 66 loci involved in blood pressure regulation. A genome-wide association study reported the >60,000 have 50 loci for hypertension and a study nearly, 90,000 individuals have an association with Arg 398 allele.<sup>25</sup> In another study, 31 new loci were identified for cardiovascular disease. Three studies reported about the research on hypertension come across 63 loci influences blood pressure, which is also responsive for variation of less than 1% in the population. A trial of 20 individuals for a drug mineralocorticoid receptor provided a statistically significant positive impact for 15 patients to treat the non-resistant hypertension while the negative impact was observed for 5 patients.<sup>26</sup>

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