Epidemiology and Genetics of Hypertension

Taposh Sarkar¹, Narinder Pal Singh²

Abstract

The prevalence of hypertension is increasing in India as well as in the world. The average prevalence of hypertension in India is 25-30%. The median prevalence of total hypertension in 2009 was 37.6% in men and 40.1% in women in U.S. Hypertension is a major risk factor for majority of patients with cardiovascular, cerebrovascular and renal morbidity and mortality. Environmental factors as well as genetic factors account for regulation of blood pressure and its control. Understanding of genetic factor may not only help in recognising those at risk but also help in treatment. Discovering hypertension susceptibility genes would help recognising those at risk for developing the disease before the expression of clinical symptoms. Genetic and epidemiological studies have suggested that essential hypertension is a polygenic and multifactorial disorder that results from genetic and/or environmental factors. In India awareness, treatment and control status of hypertension is low, with only half of the urban and a quarter of the rural hypertensive individuals being aware of its presence. In this review we have discussed epidemiology and genetics of hypertension, both the monogenic and polygenic forms.

Introduction

Hypertension is a well-known risk factor for morbidity and mortality linked with stroke, heart failure and coronary artery disease as well as progression of chronic kidney disease (CKD).¹ Regulation of blood pressure (BP) is a complex process and apart from environmental factors multiple genes likely interact to influence it. Eventhough some of the pathways of BP control have been well described in humans and experimental models²,³ identifying genes that contribute to the distribution of BP in populations and the underlying biology has proved challenging.⁴ Discovering gene variants that contribute to hypertension may not only afford better understanding of the pathophysiology of the disease but also may reveal the biochemical and physiological pathways that connect various risk factors in hypertension. Moreover, it will also help understanding the interaction between genes and environmental factors. Identifying hypertension susceptibility genes would help recognizing those at risk for developing the disease before the expression of clinical symptoms. This may lead to new therapeutic approaches, and shift the focus of management towards prevention rather than treatment. Genetic epidemiological studies have suggested that several genetic variants increase the risk for hypertension.⁵ Twins and adoption studies have indicated a greater degree of trait concordance among identical compared with dizygotic twins⁶ and among natural compared with adoptive siblings⁷ respectively, which also stress the importance of genetic factors.⁸

In the present review we have discussed the epidemiology and genetics of hypertension, both the monogenic and polygenic forms.

Definition

Hypertension in adults age 18 years and older is defined as systolic blood pressure (SBP) of 140 mmHg or greater and/or diastolic blood pressure (DBP) of 90 mmHg or greater or any level⁹ of blood pressure in patients taking antihypertensive medication.

Hypertension is also defined as values ≥140 mmHg SBP and/or ≥90 mmHg DBP, based on the evidence from RCTs that in patients with these BP values treatment-induced BP reductions are beneficial.¹⁰ Classification of hypertension by various guidelines is shown in Table 1.

Prehypertension

Prehypertension was defined as a systolic blood pressure of 120–139 mmHg and/or a diastolic blood pressure of 80–89 mmHg. The seventh report of the Joint National Committee (JNC-VII)⁹ has introduced the concept of prehypertension in the new guideline for the management of blood pressure. Recently published Guideline on hypertension-III, didn’t accept prehypertension rather than they called it high normal blood pressure because it

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Hypertension

Isolated systolic hypertension

Prehypertension

High normal 130-139 85-89

Normal 120-129 80-84

Optimal blood pressure with hypertension on the basis of average blood pressure levels, clinicians should specify presence be evaluated for clinical significance.

***Based on the average of two or more blood pressure readings taken at least on two visits after an initial screening. JNC: Joint National Committee, IGH-II: Indian Hypertension Guidelines-II, BHS: British Hypertension Society, NICE: National Institute for Health and Clinical Excellence.

Table 1: Classification of blood pressure by various guidelines

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Optimal”</td>
<td>&lt;120 &lt;80</td>
<td>&lt;120 &lt;80</td>
<td>--</td>
</tr>
<tr>
<td>Normal</td>
<td>120-129 80-84</td>
<td>&lt;130 &lt;85</td>
<td>--</td>
</tr>
<tr>
<td>High normal</td>
<td>130-139 85-89</td>
<td>130-139 85-89</td>
<td>--</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Hypertension”</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Stage I</td>
<td>140-159 90-99</td>
<td>140-159 90-99</td>
<td>≥140 ≥90</td>
</tr>
<tr>
<td>Stage II</td>
<td>160-179 100-109</td>
<td>160-179 100-109</td>
<td>≥160 ≥100</td>
</tr>
<tr>
<td>Stage III</td>
<td>≥180 ≥110</td>
<td>≥180 ≥110</td>
<td>-- --</td>
</tr>
<tr>
<td>Severe hypertension</td>
<td>--</td>
<td>--</td>
<td>≥180 ≥110</td>
</tr>
</tbody>
</table>

Isolated systolic hypertension

Grade 1 | ≥140 <90 140-159 <90 | -- |
Grade 2 | -- | -- | ≥160 ≥90 | -- |

Table 2: Recent studies (2004-2012) on prevalence of urban and rural Indian population

<table>
<thead>
<tr>
<th>First Author</th>
<th>Year</th>
<th>Place</th>
<th>Age (yrs)</th>
<th>Sample size</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deals PC</td>
<td>2004</td>
<td>Mumbai</td>
<td>≥35</td>
<td>88,635</td>
<td>47.9</td>
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<tr>
<td>Reddy KS</td>
<td>2006</td>
<td>National</td>
<td>20-69</td>
<td>19,973</td>
<td>27.24</td>
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<tr>
<td>Mohan V</td>
<td>2007</td>
<td>Chennai</td>
<td>≥20</td>
<td>2,350</td>
<td>20.0</td>
</tr>
<tr>
<td>Yadav S</td>
<td>2008</td>
<td>Lucknow</td>
<td>≥30</td>
<td>1,746</td>
<td>32.2</td>
</tr>
<tr>
<td>Momin MH</td>
<td>2012</td>
<td>Gujarat</td>
<td>≥20</td>
<td>1,493</td>
<td>30.4</td>
</tr>
<tr>
<td>Hazarika T</td>
<td>2004</td>
<td>Assam</td>
<td>≥30</td>
<td>3,180</td>
<td>33.3</td>
</tr>
<tr>
<td>Thakappan TH</td>
<td>2006</td>
<td>Kerala</td>
<td>≥30</td>
<td>2,159</td>
<td>36</td>
</tr>
<tr>
<td>Krishnan A</td>
<td>2008</td>
<td>Haryana</td>
<td>15-64</td>
<td>2,828</td>
<td>9.3</td>
</tr>
<tr>
<td>Yuvaraj BY</td>
<td>2010</td>
<td>Davangere</td>
<td>≥18</td>
<td>1,900</td>
<td>18.3</td>
</tr>
<tr>
<td>Rajasekar VD</td>
<td>2012</td>
<td>Tamil Nadu</td>
<td>≥30</td>
<td>1,905</td>
<td>19.1</td>
</tr>
</tbody>
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causes unnecessary anxiety among people.

Resistant Hypertension

Resistant hypertension is failure to achieve goal blood pressure <140/90 mmHg (or <130/80 mmHg) in patients with diabetes or CKD) in patients with hypertension who are adherent to maximal tolerated doses of an appropriate regimen consisting of three antihypertensive drugs, one of which is a diuretic.9

Controlled Resistant Hypertension

Those patients who are in accord with the definition of resistant hypertension but whose blood pressure is controlled on maximal tolerated doses of four or more antihypertensive medications.

Refractory Hypertension

In this group, patients who also meet the definition of resistant hypertension but whose blood pressure is not controlled on maximal tolerated doses of four or more antihypertensive medications.

White-coat (or Isolated Office) Hypertension

White-coat or isolated office or ‘isolated clinic hypertension’ refers to the condition in which BP is elevated in the office at repeated visits and normal out of the office, either on Ambulatory Blood Pressure Monitoring (ABPM) or Home Blood Pressure Monitoring (HBPM).

Epidemiology of Hypertension in India

In the late nineties and early twenty-first century, the prevalence of hypertension varied among different studies in India, ranging from 2-15% in urban India and 2-8% in rural India. In developing countries, it is the seventh highest contributor to premature death. Kearney et al reported that around 1 billion adults had hypertension in 2000, and this is estimated to elevate to 1.56 billion by 2025.15 There is a trend of gradual increase in the prevalence of hypertension in last six decade.16 In 2008, Tiwari et al conducted a study among labour population of Gujarat and was found that the prevalence of hypertension was 16.9% as per WHO criteria.17 In a recently published article in a rural area of Tamil Nadu, the overall prevalence of hypertension among adults was 19.1% (males-19.6% and females-18.5%),18 whereas Kokiwar et al found that the prevalence of hypertension was 19.04% in a rural community of Nagpur. A few details of the prevalence of hypertension in urban and rural India is shown in Table 2.
the prevalence of hypertension ranges between 22% and 55%. In a recent report by World Health Statistics 2012, 57 million global deaths was estimated in 2008, 36 million (63%) were due to non-communicable diseases (NCDs). The largest proportion of NCD deaths is caused by cardiovascular diseases (48%). The prevalence of hypertension for the European average was 44.2% compared with 27.6% in North America (Table 3). Olives et al from US estimated that the median prevalence of total hypertension in 2009 was 37.6% in men and 40.1% in women. Similarly, the prevalence of hypertension in England (30-45%), Canada (19.6%), China (26.6%), Australia (27%) and New Zealand (31%). An analysis of data from the 1999–2004 National Health and Nutrition Examination Survey (NHANES) over the 5 years found that the prevalence of hypertension in the USA increased from approximately 27% to 29%. Similarly another survey by NHANES from 2004–2007 revealed a high prevalence of hypertension was 47% in adults aged ≥55 years and increased to 56% in those aged 75–84 years. The complications of uncontrolled hypertension leads to diseases such as congestive heart failure, stroke, coronary artery disease, renal insufficiency, and peripheral vascular disease, which are mainly responsible for major causes of morbidity and mortality.

**Role of Genetics in Hypertension**

Essential hypertension (EH) is a polygenic and multifactorial disorder that results from genetic and/or environmental factors (Figure 1). The response to antihypertensive treatments is variable. It was found that apart from environmental factors, genetic predisposition, compliance issues and non-compatible drug combination also play an important role. Beevers et al found that around 30% of variation in blood pressure is due to genetic factors.

**Mendelian (Monogenic) Forms of Hypertension**

Adequate information obtained so far in the field of hypertension genetics came from single-gene disorders from which gene variants causing the trait were characterized. Common genetics-mediated hypertension is given in Table 4.

**Liddle’s Syndrome**

It is an autosomal dominant disorder that leads to increased

<table>
<thead>
<tr>
<th>Country</th>
<th>Prevalence, %</th>
<th>On anti-HT medications (%)</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>North America</td>
<td>27.6</td>
<td>30.4</td>
<td>24.8</td>
</tr>
<tr>
<td>United States</td>
<td>27.8</td>
<td>29.8</td>
<td>25.8</td>
</tr>
<tr>
<td>Canada</td>
<td>27.4</td>
<td>31.0</td>
<td>23.8</td>
</tr>
<tr>
<td>Europe</td>
<td>44.2</td>
<td>49.7</td>
<td>38.6</td>
</tr>
<tr>
<td>Italy</td>
<td>37.7</td>
<td>44.8</td>
<td>30.6</td>
</tr>
<tr>
<td>Sweden</td>
<td>38.4</td>
<td>44.8</td>
<td>32.0</td>
</tr>
<tr>
<td>England</td>
<td>41.7</td>
<td>46.9</td>
<td>36.5</td>
</tr>
<tr>
<td>Spain</td>
<td>46.8</td>
<td>49.0</td>
<td>44.6</td>
</tr>
<tr>
<td>Finland</td>
<td>48.7</td>
<td>55.7</td>
<td>41.6</td>
</tr>
<tr>
<td>Germany</td>
<td>55.3</td>
<td>60.2</td>
<td>50.3</td>
</tr>
</tbody>
</table>

*Age adjusted. BMI calculated as weight in kilograms divided by the height in meters squared*
resorption of sodium and water in the renal collecting tubules and hence develops to hypertension. Patients with Liddle’s syndrome are characterized by expanded plasma volume caused by excessive salt and water reabsorption in the distal nephron, resulting in low levels of plasma rennin activity (PRA), serum potassium and metabolic activity. The syndrome was come into existence due to mutations in the genes coding for the β and γ subunits of ENaC (epithelial sodium channel).\(^{50}\) The surface expression of ENaC decreases by Nedd4-2 by targeting for degradation. Hence, the mutations of Liddle’s syndrome enhance ENaC surface expression by disrupting its interaction with Nedd4-2.

**Syndrome of Apparent Mineralocorticoid Excess (AME)**

AME is an autosomal recessive disorder characterized by early onset of moderate to severe hypertension. Mune et al evaluated that patients with AME1 have insufficiency in 11β-hydroxysteroid dehydrogenase (11β-HSD) that direct to inactivation of cortisol\(^{51}\) while patients with AME2 have reduced function of the enzyme because of different mutation in the same gene. 11β-hydroxysteroid dehydrogenase Type 2 (HSD11β2) gene contains of 5 exons and has a total length of about 6.2 kb. By fluorescence in situ hybridization (FISH), Agarwal et al localized the HSD11β2 gene to chromosome 16q22.\(^{52}\)

**Glucocorticoid-Remediable Aldosteronism (GRA)**

Lifton et al in 1992 found that GRA is an autosomal dominant trait caused by a gene duplication arising from unequal crossover between the genes encoding for aldosterone synthase and 11β-hydroxylase.\(^{53}\) GRA is an increasingly recognized form of hereditary primary hyperaldosteronism. As a result, a high quantity of aldosterone, which is under the control of adrenocorticotropic hormone, will be secreted leading to increased salt and water re-absorption and rise in blood pressure. Rich et al found that most patients with GRA have normal potassium levels\(^{54}\) despite biochemical proof for primary hyperaldosteronism. One prospective study\(^{54}\) in a large pedigree with GRA revealed that normokalemia was the rule unless patients had been treated with potassium-wasting diuretics. Thus, hypokalemia lacks sensitivity as a screening test for GRA. The reason why GRA subjects have normal potassium levels is not understood, but there is not renal impairment of the actions of aldosterone.

**Mineralocorticoid Receptor (MR) Activating Mutation**

Geller et al in 2000 stated that a heterozygous gain-of-function mutation, S810L, in MR has been reported in patients with early-onset severe hypertension.\(^{55}\) Patients with the S810L mutation showed an increase in renal salt reabsorption, a marked elevation of blood pressure, and a marked suppression of aldosterone secretion, and developed hypertension before they were 20 years old. In the mineralocorticoid receptor, replacement of leucine in place of serine at codon 810 (S810L) mutations causes early-onset hypertension that is markedly worsened in pregnancy. This mutation results in constitutive MR activity and alters receptor specificity.\(^{56}\) All steroids that exhibit antagonist properties are capable to activate the mutant receptor (L810) when bound to the wild-type MR. Three pedigree members with GRA revealed that normokalemia was the rule unless patients had been treated with potassium-wasting diuretics. Thus, hypokalemia lacks sensitivity as a screening test for GRA. The reason why GRA subjects have normal potassium levels is not understood, but there is not renal impairment of the actions of aldosterone.

Table 4: Causative mutations for Mendelian forms of hypertension

<table>
<thead>
<tr>
<th>Monogenic Syndrome</th>
<th>Causative gene</th>
<th>Characteristics of mutations</th>
<th>Enzyme function</th>
<th>Inheritance</th>
<th>Chromosome</th>
</tr>
</thead>
<tbody>
<tr>
<td>GRA(^{43})</td>
<td>CYP11B1 and CYP11B2</td>
<td>Fusion gene arising unequal crossover</td>
<td>Increasing</td>
<td>AD</td>
<td>8P</td>
</tr>
<tr>
<td>Pseudo-aldosteronism(^{44})</td>
<td>SCNN1B and SCNN1G</td>
<td>Tuncation mutation in C-terminal region and missense mutations</td>
<td>Increasing</td>
<td>AD</td>
<td>16P</td>
</tr>
<tr>
<td>FHH (Gordon’s syndrome)(^{45})</td>
<td>WNK1 and WNK4</td>
<td>Deletion and missense mutations</td>
<td>Increasing</td>
<td>AD</td>
<td>12p and 17q</td>
</tr>
<tr>
<td>AME(^{46})</td>
<td>HSD11B2</td>
<td>Missense and deletion mutation</td>
<td>Decreasing</td>
<td>AR</td>
<td>16q</td>
</tr>
<tr>
<td>Hypertension exacerbated in pregnancy(^{47})</td>
<td>NR3C2</td>
<td>Missense mutation</td>
<td>Increasing</td>
<td>AD</td>
<td>4q</td>
</tr>
<tr>
<td>HTNB</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Mitochondrial Mitochondrial Mitochondrial dysfunction</td>
<td>AD</td>
</tr>
<tr>
<td>Hypertension, hypercholesterolemia and hypomagnesaemia(^{48})</td>
<td>MT-TI</td>
<td>Missense mutation</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

GRA, glucocorticoid-remediable aldosteronism; AME, syndrome of apparent mineralocorticoid excess; AD, autosomal dominant; AR, autosomal recessive; HSD11B2, gene encoding 11β-HSD2; MT-TI, mitochondrially encoded tRNA\(_{\text{Ile}}\); NR3C2, gene encoding MR; SCNN1B and SCNN1G, genes encoding β- and γ- subunits of ENaC respectively. (Reference: from Maolian G et al, 2006\(^{49}\))
Na–Cl and K+ handling. In WNK kinase family, mutation in the two members i.e. WNK1 and WNK4, cause the disease. These genes are vastly expressed in the kidney. WNK1 is located in cytoplasmic region, while WNK4 localizes to tight junctions.

The regulation of salt and water reabsorption is one of the common pathways that are involved in genetic form of hypertension. The relation between genetic variation and monogenic forms of hypertension offers insight into the more general form of hypertension especially in patients where the genetic defect has been characterized.

**Essential (Polygeneic) Form of Hypertension**

**Renin–Angiotensin–Aldosterone System (RAAS)**

One of the most commonly studied systems in relation to genetic susceptibility to hypertension is the RAAS system. One gene which has relatively produced more consistent results so far is angiotensinogen (AGT). Kunz et al in a meta-analysis review showed a connection between methionine-threonine replacement at position 235 (M235T) with an increased risk of hypertension.\(^{37}\)

The human gene for angiotensin II type 1 receptor (AGTR1) located at chromosome 3q21-25 has a length of >55 kb and composed of five exons and four introns. In a study on Mongolian population, Xu et al investigated 1099 subjects to estimate the association between ACE and environmental factors predisposing to essential hypertension claimed evidence for an interaction between the ACE DD (deletion/deletion) and ID polymorphism and cigarette smoking, alcohol drinking and BMI (body mass index).\(^{38}\) Wang et al study on Chinese Han population revealed that ACE I/D, a-adducin Gly460Trp and CYP11B2 –344C/T polymorphisms collaborate to influence SBP, suggesting these genes might indeed predispose to hypertension, especially in an ecogenetic context characterized by high salt intake.\(^{39}\) A haplotype analysis by Kumar et al showed that the T-344C and A6547G, but not the T4986C, variants of aldosterone synthase gene (CYP11B2) are linked with hypertension in females of the Anglo-Celtic population.\(^{40}\)

**G-Proteins/Signal Transduction Pathway System**

The major function of G proteins is to translate signals from the cell surface into a cell to mediate the intracellular effects of many hormones and peptides. These signalling pathways are influenced by hormones and neurotransmitters and act to control blood pressure. In β3 subunit of GTP binding protein (GNB3/C825T) a polymorphism C825T in exon 10 has been identified. This polymorphism is associated with better intracellular signal transduction and has been reported to be linked with various forms of cardiovascular risk factors, including obesity, diabetes or dyslipidemia, hypertension.\(^{41}\) In a study of Jiah et al reported a significant difference of T393C polymorphism of the Gsa gene (GNAS1) between white hypertensive and controls.\(^{62}\) However, in another study by Abe et al on Japanese population showed a marginal significant difference in the frequency of this polymorphism between hypertensives and controls.\(^{43}\)

A study on the regulator of G protein signalling (RGS2) gene in mice showed that mutant mice deficient in RGS2 gene had higher mean arterial pressure than the wild mice.\(^{63}\)

**Noradrenergic System**

The sympathetic nervous system acts through two main groups of adrenergic receptors, α and β with several subtypes, all linked to Gs proteins. The adrenergic system affects blood pressure by cardiac output and peripheral resistance regulation. The β1 adrenergic receptor (ADRB1) is a 7-transmembrane Gs protein coupled receptor. Maqbool et al found that several polymorphisms of the ADRB1 exist, but two major single nucleotide Ser49Gly and Arg389Gly are associated with BP.\(^{64}\) The Ser49Gly polymorphism is located in the extracellular amino-terminal region of the receptor, but the potential functional consequence of this polymorphism is not known.\(^{65}\) Further in β2-receptor gene, three polymorphisms (Arg16Gly, Glu27Gln and Thr164Ile) have been studied. Busjahn et al studied on normal twins and found an association between 16Gly, 27Glu/Gln and 164Ile with hypertension.\(^{66}\) A similar association was found by Bray et al between 16Gly and 27Glu/Gln with hypertension by a genome-wide linkage study.\(^{67}\)

**Ion Channels**

It is indicated by studies on Liddle’s syndrome that ENaC as a logical candidate gene for severe hypertension. A study by Baker et al in 1988 in which they found that in Black individuals, the T594M mutation of the β subunit of this gene increases the risk of hypertension\(^{68}\) while in another study in Chinese population has shown little influence on blood pressure. A sibling-pair analysis of white individuals by Wong et al indicated a linkage between systolic blood pressure and microsatellite markers on chromosome 16p12.3, a region close to the gene coding for the β and γ subunits of ENaC gene.\(^{69}\)

Few genes have been studied which code for amiloride-sensitive sodium channels (SCNN1A, SCNN1B and SCNN1G). The risk of hypertension increases only with SCNN1A G2139 allele. It was shown by sibling pair linkage analysis that SCNN1B and SCNN1G alleles are implicated in the pathogenesis of systolic blood pressure.\(^{69}\)
**Future Direction**

Despite the considerable advances that have occurred over the past few decades in the management of hypertension yet it remains one of the major epidemics in the western as well as in developing world. Thus, efforts are ongoing to develop new strategies to combat this condition.

The goal blood pressure is generally defined as <140 mmHg for systolic blood pressure and <90 mmHg for diastolic blood pressure; in some studies the goal is lowered to <130/80 mmHg for patients with diabetes mellitus or renal dysfunction, or even for all high and very high-risk patients.

For management of hypertension, renal denervation has previously been explored via surgical nephrectomy, and even radical surgical sympathectomy. It has been exposed to be an effective means of decreasing sympathetic outflow to the kidney, augmenting natriuresis and diuresis, and reducing renin release, by using surgical renal denervation without critically affecting other functions of the kidney such as glomerular filtration rate (GFR) and renal blood flow. The renal denervation procedure itself involves femoral artery catheterization, with the tip of the catheter being placed in the distal renal artery. Another technique to control refractory hypertension is arterial baroreceptors. In response to continued BP elevations the arterial blood pressures are rapidly reset, but they also buffer short-term fluctuations in BP. Devices that are used for baroreceptor stimulation have been commercialized and their pre-clinical and clinical verification are undergoing. In patients with severe hypertension refractory to drug therapy, the Rheos implantable carotid sinus stimulator has been studied. The reduction of blood pressure has been seen by using these techniques.

One of the powerful tools has been discovered to influence the expression of a specific gene in the form of gene therapy, in order to compensate for the hypoactivity or hyperactivity of a defective gene. This can be accomplished by suppression of a defective gene or by overexpression of a normal gene. In fact, both approaches have been used for the control of hypertension. For example, study by Chao and collaborators in adult rats have been unbeaten in reversing hypertension by over-expressing the vasodilatory genes: atrial natriuretic peptide (ANP), kallikrein, adrenomedulin, and endothelial nitric oxide synthase. It has been confirmed by their studies that delivery of each gene, either by using viral delivery or by naked DNA, consequences in an outstanding lowering of blood pressure (BP) that was short-lived in nature, lasting somewhere from 6 to 12 weeks in different models of hypertension. Similarly, delivery of human endothelial nitric oxide synthase plasmid DNA into the spontaneously hypertensive rat (SHR) stimulated noteworthy increases in urinary and aortic cGMP and urinary and serum nitrite/nitrate, without a significant effect on body weight, heart rate, water intake, or food consumption.

Another approach has been developed that is “antisense” to target the major vasoconstrictor pathways. The fundamental principle behind the antisense approach is that it obstructs the formation of the targeted protein rather exclusively either at the transcriptional or translational level.

**Conclusion**

The prevalence of high blood pressure is increasing all over the world. Controlling of blood pressure (BP) is a complex process and multiple genes likely collaborate to influence it besides environmental factors. The underlying cause of hypertension is poorly understood. Only a little proportion of hypertensive patients convey demonstrated genetic abnormalities. These incorporate mutations in the 11-β-hydroxy steroid dehydrogenase gene and mutations in certain renal ion channels such as those found in Liddle’s and Gordon’s syndromes and others were glucocorticoid-remediable aldosteronism, mineralocorticoid receptors and pseudohypoaldosteronism type II. However, in majority of patients, the cause of hypertension is not known and falls into the group of “primary hypertension”. In this scenario few genes were targeted like RAAS, G-proteins/signal transduction pathway system, noradrenergic systems and ions channels. Understanding their genetic mutations can throw further light in understanding the management of hypertension.

**References**


hypertension caused by mutations in the β subunit of the epithelial sodium channel. 


