Review Article

Overweight, air and noise pollution: Universal risk factors for pediatric pre-hypertension

Roya Kelishadi 1, Parinaz Poursafa 2, Kasra Keramatian 3

Abstract

Pediatric pre-hypertension (pre-HTN) has a complex multifactorial etiology. Although most cases are secondary to other disorders, a substantial number of children and adolescents have primary or essential HTN and pre-HTN. The gene-gene and gene-environment interactions should be considered in this context. The strong relationship of pre-HTN with environmental factors such as air pollution, noise pollution and passive smoking and obesity suggest that its prevalence will be escalating.

Exposure to ambient particulate matters may increase blood pressure (BP) within hours to days. The underlying biological pathways include autonomic nervous system imbalance and arterial vascular dysfunction or vasoconstriction because of systemic oxidative stress and inflammation. Likewise, tobacco smoke exposure of pregnant mothers increases systolic BP of their offspring in early infancy. Parental smoking also independently affects systolic BP among healthy preschool children. Noise exposure, notably in night, is associated with catecholamine secretion, increased BP and a pre-HTN state even in pre-school age children.

Excess weight is associated with dysfunction of the adipose tissue, consisting of enlarged hypertrophied adipocytes, increased infiltration by macrophages and variations in secretion of adipokines and free fatty acids. These changes would result in chronic vascular inflammation, oxidative stress, activation of the renin-angiotensin-aldosterone system and sympathetic response, and ultimately to pre-HTN from childhood.

Prevention and control of the modifiable risk factors of pre-HTN from prenatal period can have long-term health impact on primordial and primary prevention of chronic non-communicable diseases. This review presents a general view on the diagnosis, prevalence and etiology of pre-HTN along with practical measures for its prevention and control.

KEYWORDS: Prevention, Blood Pressure, Pre-hypertension, Genetics, Environment, Children.
high BP significantly damages vital organs function in the future life of children and adolescent, but also pre-hypertension (pre-HTN) has the same harmful effects.\textsuperscript{9,10,12,13} The Fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents highlighted that all children aged above 3 years who are seen in a medical setting should have their BP measured.\textsuperscript{14} It also illustrated the concept of pre-HTN after that the same term was developed for adults by the Joint National Committee on prevention detection evaluation and treatment of high blood pressure seventh report (JNC7). This term is used when a person's BP is elevated above normal but not to the level considered to be HTN.\textsuperscript{15}

Given the increasing evidence on tracking of BP from childhood into adult life, the relative contributions of genetic, prenatal, environmental, biological and behavioral determinants to pediatric pre-HTN should be underscored. This review emphasizes on the importance and determinants of pre-HTN among children and adolescents, and highlights the modifiable factors that may be effective in primordial prevention of many chronic non-communicable diseases.

For this review, we identified studies published in the English language from 1990 to 2011, by a World Wide Web-based literature search using PubMed, Medline, Ovid MEDLINE(R) in process and other non-indexed citations, Allied and Complementary Medicine (AMED), Cumulative Index to Nursing and Allied Health Literature (CINAHL), Scopus, CAB Abstracts, and Global Health. The following search terms were used: blood pressure, hypertension, hypertensive, high blood pressure, pre-hypertension, lifestyle, environment, genetics, children, adolescents, and prevention. Data on study design and location, confounding factors, health outcomes, and study findings were extracted from the selected studies. We also used secondary references cited by the articles recognized in the primary search.

1. Diagnosis of pre-HTN in children and adolescents

The diagnosis of pre-HTN needs multiple measurements, taken at least in three occasions over a period of time. Home and ambulatory BP measurements are more precise, but are recommended for special cases. In children and adolescents, home BP is lower than daytime ambulatory BP. This difference may be because of the daytime physical activity of this age group. Stage I hypertension is defined as a mean BP level from the 95\textsuperscript{th} percentile to 5mmHg above the 99\textsuperscript{th} percentile. Stage II hypertension is considered as an average BP exceeding 5mmHg above the 99\textsuperscript{th} percentile.\textsuperscript{6, 14}

The BP percentiles are constructed in some countries, and have reported slightly higher BP levels in children living in Northern Europe\textsuperscript{16, 17} and South Asia\textsuperscript{18} than those living in the US,\textsuperscript{6, 14} however a national study in Iran revealed reference curves consistent with the US curves.\textsuperscript{19}

During growth, BP increases with age and body size; thus the accurate diagnosis of abnormal BP levels requires the use of standardized charts by age, gender and height.\textsuperscript{6, 14} Despite the report of Collins et al. which challenged the recent method of diagnosis of these disorders in the pediatric age groups,\textsuperscript{20} clinicians use the national high blood pressure education program working group guideline.\textsuperscript{6, 14, 21} In accordance with this guideline, pre-HTN is defined as the average systolic or diastolic blood pressure between 90\textsuperscript{th} and 95\textsuperscript{th} percentile in more than three different visits, and HTN as the average BP values more than 95\textsuperscript{th} percentile. Quantities lower than 90\textsuperscript{th} percentiles are considerate as the normal BP. The definition of pre-HTN is similar in adolescents of all ages, and is considered as BP > 120/80 mmHg.\textsuperscript{6, 14, 21, 22}

The importance of pre-HTN in children and adolescents has different aspects. While increasing evidence is now available on the prevalence of pre-HTN and HTN in the pediatric age group and on escalating number of the cases of essential HTN in adolescence, there is
also evidence of BP tracking, indicating that children and adolescents with pre-HTN tend to maintain that position over time.\textsuperscript{6,22-25}

2. Prevalence of pre-HTN in the pediatric age group

Limited evidences exist on the prevalence of pre-HTN in children and adolescents. A summary of different results is presented in Table 1.\textsuperscript{9,10,12,26-40} This prevalence has a wide range, and is usually about 4\%, but it has been reported as high as 15.7\% in adolescents.\textsuperscript{39} Serial BP measurement over time showed that 14\% of adolescents with pre-HTN developed HTN in 2 years, which shows an incidence rate of about 7\% per year for HTN. In the same study, after two years of follow up, 43\% of girls and 68\% of boys with high risk BP values developed pre-HTN.\textsuperscript{4}

3. Etiology of pre-HTN in children and adolescents

Pediatric HTN and pre-HTN have a complex multifactorial etiology. Although most cases are secondary to causes as renal, cardiovascular or endocrine disorders, a substantial number of children and adolescents are currently diagnosed with primary or essential HTN and pre-HTN.\textsuperscript{41} Some of the most important etiologies are as follows:

3.1. Genetic factors

There is a growing body of evidence in detecting mutations and different combinations of genetic variations which may cause HTN and pre-HTN. Potentially variations were identified, which were associated with quantitative differences in the expression of multiple genes such as the differences in expression of the genes coding for the angiotensin-converting enzyme and for the natriuretic peptide receptor.\textsuperscript{22,42-48} However the etiology is more complex and the gene-gene and gene-environment interactions should be considered in this context.\textsuperscript{49}

3.2. Environmental factors

Exposures to various environmental factors before and after birth have harmful effects on cardiovascular system.\textsuperscript{50} Various environmental risk factors are identified for pre-HTN, the most important ones being air pollution, noise pollution and second-hand smoking.

3.2.1. Air pollution and pre-HTN

A growing body of evidence exists about the effect of air pollutants, notably particulate matter (PM) on pre-HTN. This association was found to be independent of aerologic factors like weather, temperature or humidity and of major cardiovascular risk factors such as age, diabetes, dyslipidemia and obesity.\textsuperscript{51,54}

Accumulating evidences suggest that exposure to ambient levels of PM may increase BP within hours to days and can result in a prohypertensive response. The underlying biologic pathways include autonomic nervous system imbalance and arterial vascular dysfunction or vasoconstriction because of systemic oxidative stress and inflammation.\textsuperscript{22,55,56} Given the harmful effects of air pollutants, notably PM, on various organs and on underlying mechanisms of atherosclerosis and endothelial dysfunction from childhood,\textsuperscript{57-64} preventive measures should be considered from early life. The Multi-Ethnic Study of Atherosclerosis showed that traffic-related exposure may increase systolic BP, and in turn left ventricular mass index. The increase in this index has been consistent with 5.6 mmHg elevation in BP.\textsuperscript{65-67} Exposures to air pollutants other than PM, arsenic, lead, cadmium, solvents, and pesticides have also been linked to pre-HTN.\textsuperscript{68}

3.2.2. Passive smoking and pediatric pre-HTN

The harmful effects of secondhand smoke on cardiovascular system are comparable to that of smoking.\textsuperscript{69} Some studies have documented the association of exposure to tobacco smoke with elevated BP in children and adolescents. Tobacco smoke exposure of pregnant mothers has a considerable effect on increasing systolic BP of their offspring in early infancy.\textsuperscript{70} A recent large population-based study showed that parental smoking independently affects systolic BP among healthy preschool children even after correction for other risk factors, such as body mass index, parental hypertension, or
### Table 1. Summary of studies on the prevalence of pediatric pre-hypertension: 1990-2011

<table>
<thead>
<tr>
<th>Reference</th>
<th>Location</th>
<th>Population</th>
<th>Aims</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stabouli S et al., 2009</td>
<td>Athens, Greece</td>
<td>124 children and adolescents (5 to 18 y)</td>
<td>Investigate the left ventricular mass index (LVMI) and left ventricular hypertrophy (LVH) among pre-hypertensive and hypertensive children.</td>
<td>Hypertensive and pre-hypertensive subjects had significantly higher LVMI as well as more prevalence of LVH than normotensive.</td>
</tr>
<tr>
<td>Genovesi S et al., 2008</td>
<td>Milan, Italy</td>
<td>75 children (9.7 ± 0.2 y) subdivided into three groups of normotensive, pre-hypertensive and hypertensive</td>
<td>Assessment of RR intervals and baroreflex impairment</td>
<td>Hypertensive and pre-hypertensive children display a marked baroreflex impairment</td>
</tr>
<tr>
<td>Lubrano R et al., 2009</td>
<td>Rome, Italy</td>
<td>cohort study 146 children with pre-HTN 104 normal blood pressure, (9.12 ± 3.28 y)</td>
<td>The effect of Pre-HTN on renal function</td>
<td>Pre-hypertensive group had higher proteinuria and lower GFR</td>
</tr>
<tr>
<td>Din-Dzietham R et al., 2007</td>
<td>United states</td>
<td>National survey data from 1963 to 2002. 8- to 17-year-old non-Hispanic blacks and whites and Mexican Americans</td>
<td>The BP, pre-HBP, and HBP trends between 1963 to 2002 The association between BP and sex, ethnic and weight</td>
<td>1) The BP, pre-HTN, and HTN trends were downward from 1963 to 1988. 2) Non-Hispanic blacks and Mexican Americans had a greater prevalence of HTN and pre-HTN than non-Hispanic whites 4) Males had a greater prevalence of pre-HTN and HTN than females 4.9% were pre-hypertensive and 4.9% were hypertensive and it's strongly associated with the obesity</td>
</tr>
<tr>
<td>Salman Z et al., 2010</td>
<td>Khartoum, Sudan</td>
<td>304 children (6-12 y)</td>
<td>prevalence of HTN and Pre-HTN and its association with obesity</td>
<td>1) Pre-HTN in 12.3%. HTN in 5.9% of children. 2) more urban have HTN and more rural children have Pre-HTN 3) HTN and Pre-HTN are more in higher BMI 13.6% of boys and 5.7% of the girls aged were classified as Pre-HTN, Both obese boys and girls had higher rate of Pre-HTN and HTN.</td>
</tr>
<tr>
<td>Sharma A et al., 2010</td>
<td>Shimla, northern India</td>
<td>1085 students aged 11-17 years</td>
<td>prevalence of HTN and PRE-HTN in comparison with urban and rural and in relation to obesity</td>
<td>1) Pre-HTN in 12.3%. HTN in 5.9% of children. 2) more urban have HTN and more rural children have Pre-HTN 3) HTN and Pre-HTN are more in higher BMI 13.6% of boys and 5.7% of the girls aged were classified as Pre-HTN, Both obese boys and girls had higher rate of Pre-HTN and HTN.</td>
</tr>
<tr>
<td>Ostchega Y et al., 2009</td>
<td>United states</td>
<td>8-17 years from the National Health and Nutrition Examination Surveys (NHANES)</td>
<td>PRE-HTN and HTN estimation during 2003-2006</td>
<td>3.4% had pre-HTN vs. 3.6% HTN HTN and pre-HTN were frequently undiagnosed</td>
</tr>
<tr>
<td>Hansen ML et al., 2007</td>
<td>Northeast Ohio</td>
<td>14,187 children and adolescents aged 3 to 18 years. cohort study June 1999 until September 2006</td>
<td>determine the frequency of undiagnosed HTN and PRE-HTN</td>
<td>Pre-HTN was 7.6% overweight was associated with HTN but not pre-HTN. Obesity was associated with both of them.</td>
</tr>
<tr>
<td>Salvadori M et al., 2008</td>
<td>Canada</td>
<td>675 children (aged 4-17 years) during the year 2004</td>
<td>Evaluation of the association between overweight and obesity with pre-HTN and HTN in the rural children</td>
<td>Pre-HTN was 7.6% overweight was associated with HTN but not pre-HTN. Obesity was associated with both of them.</td>
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Table 1. Continue

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<tbody>
<tr>
<td>Diaz A et al., 2010</td>
<td>Argentina</td>
<td>331 children(5-11) and adolescents(12-18 y) rural students</td>
<td>prevalence of HTN, sedentary lifestyle, over-weight, and obesity</td>
<td>Pre-HTN was detected in 1.9% and 1.7% of children and adolescents. Pre-HTN was 3.6% and HTN 2.7%. Only one pre-hypertensive child versus all hypertensive ones had family history of HTN Pre-HTN 10% and HTN 10.6%. The higher prevalence of cardiovascular risk factors associated with pre-HTN and HTN</td>
</tr>
<tr>
<td>Aglony IM et al., 2009</td>
<td>Santiago, Chile</td>
<td>112 children (6-12 y)</td>
<td>Assessment of blood pressure, cardiovascular risk factors and family history in healthy children</td>
<td>HTN prevalence and cardiovascular risk factors association</td>
</tr>
<tr>
<td>Juarez-Rojas JG et al., 2008</td>
<td>Mexico City</td>
<td>1846 students (12 to 16 years old)</td>
<td></td>
<td>Pre-HTN and HTN increased 6.38% and 8.13% in children and adolescents respectively</td>
</tr>
<tr>
<td>Culhane-Pera KA et al., 2009</td>
<td>Hmong refugees Thailand</td>
<td>988 refugees (0-20 y) June 2004-March 2006</td>
<td>Prevalence of cardiovascular risk factors</td>
<td>Pre-HTN : 9.6% HTN: 8.2%</td>
</tr>
<tr>
<td>Liang YJ et al., 2010</td>
<td>China</td>
<td>8247 children and adolescents (6-17 y)</td>
<td>observe the trends in BP during 1991 to 2004</td>
<td></td>
</tr>
<tr>
<td>Chiolero A et al., 2007</td>
<td>Switzerland</td>
<td>5207 school children (12.3 ± 0.5 y) 2005/2006</td>
<td>Prevalence of pre-HTN and HTN</td>
<td>Pre-HTN:13.3% HTN: 11.4 (first visit) &amp; 2.2% (third visit)</td>
</tr>
<tr>
<td>Di Bonito P et al., 2009</td>
<td>Naples, Italy</td>
<td>447 obese and 131 normal-weight children</td>
<td>prevalence of pre-HTN in obese children</td>
<td>Pre-HTN observed in 17.7% of obese children and in 1.5% of controls. Boys were more likely to have pre-HTN.</td>
</tr>
<tr>
<td>McNiece KL et al., 2007</td>
<td>Houston, United states</td>
<td>6790 adolescents (11-17 y) 2003 to 2005</td>
<td>prevalence of HTN and pre-HTN</td>
<td>1) At first visit, 9.5% had pre-HTN, and 9.4% HTN. At third visit, 15.7% were pre-hypertensive and 3.2% hypertensive 2) HTN and pre-HTN prevalence were increased in parallel with increasing the BMI</td>
</tr>
<tr>
<td>Falkner B et al., 2008</td>
<td>Philadelphia, United states</td>
<td>8533 high school students (13 to 15y)</td>
<td>Evaluate the progression of pre-HTN to HTN</td>
<td>17.22% had pre-HTN, 14% of boys and 12% of girls had HTN 2 years later. Overall, 7% per year.</td>
</tr>
</tbody>
</table>

birth weight. Likewise, a family-centered prospective study revealed this association among children and adolescents. This widespread and modifiable risk factor should be considered in primordial and primary prevention of pre-HTN.

3.2.3. Noise pollution and pre-HTN

The cardiovascular effects of environmental noise, notably on high BP, are well documented and rank second in terms of disability-adjusted life year (DALYs) after annoyance. It is also documented that environmental noise exposure may be associated with elevated BP in young adults, especially in female individuals.

Night time noise has an effect on our blood pressure more than day time noise. The HYENA (Hypertension and Exposure to Noise near Airports) study was a large study conducted
among individuals who had lived at least 5 years near any of six major European airports. It found significant exposure-response relationships between night-time aircraft and average daily road traffic noise exposure and elevated BP. Monitoring BP showed that systolic BP increased by 6.2 mmHg and diastolic BP by 7.4 mmHg. The association of noise pollution with increased BP remained significant even after adjustment for major confounders as health, socioeconomic and lifestyle factors including diet and physical activity. Noise exposure is associated with increased catecholamine secretion. In children, in addition to impairing reading comprehension and long-term memory, chronic noise exposure may be associated with increased BP and a pre-HTN state. Such association is reported even in pre-school age children.

Some changes in BP levels cannot be explained by well-known determinants as anthropometric measures and lifestyle factors. For instance, comparison of data from 4 waves of the Korean National Health and Nutrition Examination Survey between 1998 and 2008 among children and adolescents with 10 to 19 years of age revealed significant decrease in mean BP as well as in the prevalence of pre-HTN and HTN. These changes were not explained by secular trend of childhood obesity, cigarette smoking, physical activity, dietary habits, sociodemographic factors and psychological factors as perceived stress and sleep duration. Such findings may be confirmatory evidence of the underlying role of environmental factors on BP levels and pre-HTN state in children and adolescents.

3.3. Gene-environment interaction and pre-HTN
The interaction of gene and environment on the development of many chronic diseases and their risk factors is well-established. The discrepancies of human genome and modern lifestyle can, at least in part, explain the ongoing epidemics of chronic non-communicable diseases.

Likewise, such interaction may have a pivotal role in the development of pre-HTN. A growing body of evidence exists about the link between fetal programming and pre-HTN later in life. The fetal origins of adult disease is related to insults to epigenetic modifications of genes. Such epigenetic process of establishing future diseases may affect some genes responsible for fetal and placental growth.

It is suggested that environmental changes during the prenatal and perinatal periods may be associated with altered gene expression by epigenetic mechanisms resulting in pre-HTN, HTN, and other chronic diseases.

The association of environmental fetal programming is documented in young children; it is shown that in 6-year-old children born at full term, intrauterine growth retardation was linked to pre-HTN. Different mechanisms are considered in this regard, one of them is about the role of oxidative stress. A recent experimental study showed that the intrauterine environment modifies oxidative pathways of gene expression in fetal kidneys, and this may be a mechanism of pre-HTN.

It is also suggested that fetal programming of pre-HTN may be mediated by the fundamental role of hyperinsulinism and hyperleptinemia.

Various factors as maternal obesity, dietary habits in pregnancy, and gestational diabetes are considered to be the underlying mechanism of restricted fetal growth, and in turn of pre-HTN. Of special concern in this context is the association of environmental pollutants and other chemical toxins, which may result in intrauterine growth retardation and its sequels. Environmental pollutants may influence vital cellular functions during critical periods of fetal development, and may change the structure or function of vital organs. Developmental epigenetics may lead to "adaptive" phenotypes to respond the needs of the later-life environment. Exposure to environmental pollutants and toxic chemicals may interfere with these programmed adaptive changes, and eventually may result in considerable increase in various disorders as pre-HTN.

3.4. Overweight and pediatric pre-HTN
Excess weight is associated with dysfunction of
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the adipose tissue, consisting of enlarged hypertrophied adipocytes, increased infiltration by macrophages and variations in secretion of adipokines and free fatty acids. These changes would result in chronic vascular inflammation, oxidative stress, activation of the renin-angiotensin-aldosterone system and sympathetic response, and ultimately to pre-HTN. The association of overweight with pre-HTN and HTN in the pediatric age group is well-documented.

A birth cohort demonstrated that maternal pre-pregnancy weight and BMI, and weight at the end of pregnancy are found to be positively associated with both systolic and diastolic BP in adolescent subjects of both sexes; maternal height was positively associated with systolic BP only among males.

The strong association of elevated BP with excess weight along with the childhood obesity epidemic has led to increase in the prevalence of the cases of pediatric HTN. Comparison of national data in the US revealed an increase in mean systolic and diastolic BP levels, and an overall increase in the prevalence of pre-HTN and HTN in children and adolescents.

Considering the rapidly escalating trend of childhood obesity, it can be estimated that the population prevalence of pre-HTN and HTN will be increasing from childhood to adulthood. This is of crucial importance for low- and middle-income countries facing increasing levels of childhood obesity as well as an emerging epidemic of non-communicable diseases.

3.5. Lifestyle factors associated with pediatric pre-HTN

The pre-HTN state during childhood and adolescence is associated with various lifestyle factors. Although smoking may be associated with elevated BP, but such evidence is limited in the pediatric age group. Diet and physical activity are known a pivotal role in the development, prevention and control of pediatric pre-HTN. Their impact may begin from early life.

Various factors have been considered in this regard:

3.5.1. Dietary factors in infancy

Diet is known to be associated with mean BP level, and pre-HTN; this association is documented from early life. Infant-feeding may have lifelong health impact. The protective role of breast feeding against chronic diseases and cardiometabolic risk factors, including elevated BP, is well-established. Accumulating evidence exists on the protective effect of breast feeding during infancy on BP and pre-HTN in later life.

Results of systematic reviews and meta-analyses confirmed the protective role of breast feeding against elevated BP in later life. Although, the correlations were not strong, but even such small reduction in BP associated with breastfeeding could confer important benefits at population level.

A birth cohort showed that after 7.3 years of follow up, children who were bottle-fed during infancy had significantly higher systolic BP than those who were breast-fed. However, some studies have shown small effects of breast feeding on children’s BP, and have suggested that such effect may become more evident during adolescence.

In addition to the beneficial effects of breast feeding for future BP of infants, it may have protective effects against elevated BP for mothers. A recent study in Finland found that 16-20 years after pregnancy, women who had breast-fed for less than 6 months had higher total body fat and cardiometabolic risk factors than mothers who had breast-fed for longer than 6 months or for longer than 10 months. The protective long-term effects of duration of postpartum lactation on risk factors including systolic and diastolic BP were independent of pre-pregnancy weight and BMI, menopausal status, smoking status, level of education, participation in past and present leisure-time physical activity and current dietary energy intake.

The type and the beginning time of complementary foods may have lifelong health impacts.

One of its aspects is the intake of sodium (salt), and related harmful effect on the devel-
oping kidneys and blood pressure. One of the recent evidences in this regard came from a large cohort of 8-month-old infants in the UK. It showed that 70% of infants consumed more than 400 mg sodium per day, which is the maximum UK recommendation for sodium intake in infants.\textsuperscript{141}

Given the suggested effect of salt intake from infancy to adulthood on BP, body weight and energy balance,\textsuperscript{142} high sodium intake by complimentary foods may increase the cases of pre-HTN in the future.

The important role of taste preference should be taken into account. A recent study showed that healthy and low-sodium foods can be simply introduced in the diet of most infants.\textsuperscript{143} Usually the taste preferences in new food acceptance in early life may persist lifelong, and may have long-term health effects. Pediatricians have a pivotal role in introducing healthy complimentary foods to families;\textsuperscript{144} and less-educated mothers need to be learned about infant feeding practices.\textsuperscript{145}

3.5.2. Diet in childhood and adolescence

Different guidelines have suggested low sodium intake in childhood and adolescence for prevention of pre-HTN and HTN.\textsuperscript{146-148} However, the current salt intake is far in excess of nutritional requirements in children and adolescents of many populations.\textsuperscript{126,149-153} This high intake is reported even in very young children with 3 years of age.\textsuperscript{154}

Of special concern is that the high sodium content is not limited to unhealthy foods as snacks and processed foods, those foods as bread, cheese and cereals considered as healthy with recommendation of daily consumption, are of main hidden sources of salt intake among children and adolescents.\textsuperscript{155}

Various types of studies have confirmed the effect of salt intake and pre-HTN in the pediatric age group. A large population-based study in the UK showed that the increase in salt intake by 1g in children is associated with 0.4 mmHg rise in systolic BP and 0.6 mmHg rise in pulse pressure.\textsuperscript{156}

It is also documented that in addition to the direct association of salt intake on BP, excess dietary sodium intake would affect thirst and may increase consumption of sugary beverages by children and adolescents; and in turn, it would increase the likelihood of obesity and pre-HTN.\textsuperscript{157}

A meta-analysis of controlled trials assessed the effect of reducing salt intake on BP in children and adolescents demonstrated that a modest reduction in salt intake resulted in immediate decline in BP level.\textsuperscript{158}

However, the effects of low-sodium intake on pre-HTN are controversial, and may be not generalizable. A Cochrane review suggested that the effect of low versus high sodium intake on blood pressure was greater in Black and Asian patients than in Caucasians. Magnitude of the effect in Caucasians with normal blood pressure does not warrant a general recommendation to reduce sodium intake.\textsuperscript{159}

On the other hand, some harmful effects of lowering salt intake are reported. In a recent study among healthy participants, low-salt diet was independently associated with an increase in insulin resistance.\textsuperscript{160}

The dietary recommendations for prevention and control of pediatric pre-HTN are not limited to reducing the salt intake. Findings of the 8-year follow up of children initially 3 to 6 years of age in the prospective Framingham Children's Study showed children who consumed more fruits and vegetables or more dairy products during the preschool age had smaller yearly increase in systolic BP in subsequent years. At early adolescence, children with higher intakes of fruits and vegetables and dairy products had a lower mean systolic BP than those with either high intake of one of these food groups or those with low intake of them. This longitudinal study confirmed that a diet rich in fruits, vegetables, and dairy products may have beneficial effects on BP during childhood.\textsuperscript{161} This type of diet is consistent with the classic Dietary Approaches to Stop Hypertension (DASH) including a diet high in fresh fruits, vegetables, whole grains, and low-fat dairy products, recommended for adults.\textsuperscript{162}
The beneficial effects of a DASH-type diet on cardiometabolic risk factors of children and adolescents were documented too. A large national study in the US showed that after 10 years of follow up, adolescent girls with diet more close to the DASH eating pattern had smaller gains in BMI. Trials with dietary interventions using the DASH-type diet showed favorable results in controlling pre-HTN state in diabetic and non-diabetic adolescents. These findings highlight the need to underscore the intake of fruits, vegetables, fiber and dairy in the diets of children and adolescents.

3.5.3. Physical activity and pre-HTN
Physical activity is known to positively moderate BP. There is a large body of evidence about the association of physical activity and lower cardiovascular risk factors, including pre-HTN and HTN. A study among young children showed that physical activity was independently associated with lower BP even in prepubertal children.

A recent systematic review confirmed the association of physical activity with lower BP in children, and emphasized on the role of physical fitness on prevention and control of cardiovascular risk factors in children.

Although it is well documented that sedentary behaviors are associated with pre-HTN, but a recent study among adolescents demonstrated various correlations between different types of sedentary activities and BP levels. It showed that after adjusting for confounders, while each hour per day spent in screen time, watching TV and playing video games was associated with a significant increase in diastolic BP, each hour per day spent reading was associated with a decrease in systolic and diastolic BP.

Another national study in the US revealed that high TV use, but not high computer use, and lack of moderate-to-vigorous intensity physical activity was associated with cardiometabolic risk factors among children and adolescents. Office- and population-based interventions have demonstrated that pre-HTN may be reversible by increase in physical activity.

Among different types of physical activities, aerobic exercises are found to be useful for controlling pre-HTN. Likewise, this kind of exercise has been successful in reducing systolic and diastolic BP among children and adolescents with pre-HTN and HTN.

In general, a combination of lifestyle change including healthy dietary pattern and exercise training may improve pre-HTN state and vascular function in children and adolescents.

Conclusion
Childhood onset of adult non-communicable diseases has become a substantial health problem. The strong relationship of pre-HTN with environmental factors and obesity along with the increasing environmental pollution and the childhood obesity epidemic suggest that the population prevalence of pediatric pre-HTN will be escalating, and there is already evidence that this trend is proceeding. Physicians and health professionals who care for children and adolescents should incorporate screening of adult non-communicable diseases into their practice. Prevention and control of pediatric pre-HTN is of crucial importance in primary prevention of such chronic diseases. Prevention and control of its modifiable risk factors such as air and noise pollution, passive smoking, overweight and unhealthy lifestyle, along with primordial prevention by good pregnancy care for prevention of low birth weight, encouraging breast feeding, and using healthy complimentary foods during infancy can impact the overall health of children and adolescents, as well as the prevention of chronic non-communicable diseases. Better knowledge on the etiology of these disease states will help preventive and targeted therapies.
Conflict of Interests
Authors have no conflict of interests.

Authors' Contributions
RK planned and conducted the review, wrote and finalized it, PP and KK assisted in planning, conducting and writing the review. All authors read and approved the final draft of the paper.

References


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