

The management of prehypertension in young adults

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ABSTRACT

يتراوح معدل الإصابة بضغط الدم في مرحلة ما قبل المرض (ضغط الدم 120-139 و / أو 80-89 ملم زئبق) لدى الشباب في جميع أنحاء العالم من حوالي ~37.5% إلى 77.1%. أن تحديد المجموعات المعرضة للإصابة بضغط الدم في مرحلة ما قبل المرض لدى البالغين يعد أمرًا مفيدًا للعلاج المبكر والفعال وللحد من حدوث ارتفاع ضغط الدم في المستقبل وتلف الأعضاء. نلخص في هذا التقرير الخصائص الوبائية، وطرق علاج المرض، وخصائص تطور المرض لوضع قاعدته أساسية لتطوير طرق العلاج المستهدف للشباب البالغين الذين يعانون من مرحلة ما قبل ارتفاع ضغط الدم.

The incidence of prehypertension (blood pressure 120-139 and/or 80-89 mm Hg) in young adults worldwide ranges from ~37.5% to 77.1%. Identifying high-risk groups of prehypertension in young adults is helpful for early and effective interventions and treatments to reduce the occurrence of future hypertension and organ damage. This review summarized the epidemiological characteristics, disease intervention measures, and disease progression characteristics of prehypertension to provide a basis for the development of targeted intervention measures for young adults with prehypertension.

Keywords: pre-hypertension, young adults, blood pressure

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Epidemiological data shows that the incidence of prehypertension (HN) (blood pressure 120-139/80-89 mm Hg) ranges from ~37.5% to 77.1% in adults under 44 years old,¹⁻³ especially in those with high uric acid levels,⁴ obesity,⁵ and impaired baseline blood sugar.⁶ Untreated prehypertensive individuals are thought more probably to developing HN,^{7,8} coronary heart disorder (CHD)⁹⁻¹¹ and renal disorder.^{12,13} The rates of diagnosis are consistently low in young adults (15-44 years old),^{14,15} which greatly increases the difficulty in the development and implementation of intervention strategies for HN and may lead to rapid onset of uncontrolled diseases in old age. In addition, young adults are unique and have different lifestyle practices, comorbid conditions, and disease characteristics.

To reduce the burden of CHD and end-stage renal failure (ESRF), it is necessary to summarize sufficient studies to provide convincing evidence for formulating interventions for prehypertensive youth. Some reviews analyzed the pathogenesis and intervention strategies for patients with HN, but whether these strategies are applicable to young adults is still uncertain. Therefore, it is vital to know the risk factors and intervention measures for HN in young adults.

Epidemiology. Domestic epidemiological status. Prehypertension is widely distributed around the world and has become one of the most important diseases threatening human health, especially young adults. Prehypertension may be affected by different social and demographic factors, such as altitude, lifestyle, and ethnic group. Prehypertension is widespread among young Chinese adults, except for the Miao, Tibetan and Tujia ethnic groups. A study that explored the incidence of HN in different parts of China showed that the rate of HN is up to 48% in Northeast China (47.7% in men and 33.6% in women),¹ which may be associated with cold weather and high-salt diets. However, many studies in recent years have suggested that the prevalence rate of HN is almost as high in Guangdong Province in South China, despite low-sodium diets.¹⁶ Prehypertension is also common in the She minority (35.9%) in the hilly region of Fujian Province¹⁷ and the mountainous regions in Chongqing and the central plain (55.17%).¹⁸

Prehypertensive morbidity is 63.2% in males and 47.2% in females¹⁹ and show a significant upward trend in both gender.^{20,21}

Overseas epidemiological status. Outside of China, HN is widespread in one-quarter of Indian adults who aged 18-40 years.²² Additionally, studies showed that the prehypertensive rate was 19% among college students in Southeast Asia²³ and 44.9% among young adults in Arab countries.²⁴ Prehypertension used to be rare in African populations, but it is now one of the most common cardiovascular disease (CVD) and accounts for almost 40% of all diseases in Africa.²⁵ A study with a large sample size suggested that the incidence of HN ranges from 37.5% to 42.5% in different regions and countries in Africa.²⁶ Data on HN in the United States are limited, but available studies had suggested that the rates of HN decreased slightly from 81.5% in 1999 to 77.7% in 2012.²⁷ In addition to areal variation, many social and demographic characteristics are significantly correlated with HN. For example, the incidence of HN was reported to be 55.3% in American football players²⁸ and 42.9% in police constables in a district of India,²² both of which are higher than that in the general young population. Prehypertensive morbidity is also significantly increased in young adults who have low incomes, low social status,²⁹⁻³¹ and a family history of HN.³²

Risk factors for prehypertension. Obesity. The possible association between overweight and/or obesity and HN in young adults has been confirmed in several studies. A survey showed that body mass index (BMI) was 22.5 ± 3.2 cm, waist circumference (WC) was 80.5 ± 8.5 cm and hip circumference (HC) was 94.0 ± 7.9 cm in prehypertensive young adults; BMI was 21.6 ± 3.2 cm, WC was 76.3 ± 7.8 cm, and HC was 91.3 ± 7.8 cm in the general young population. And HN was more likely to occur in populations with central obesity (odds ratio (OR)=1.9, 95% confidence interval (CI)=0.8-4.7).³³ A cross-sectional study of 4649 college students in Southeast Asia showed that obesity increased the probability of HN (OR=2.28, 95% CI=1.84-2.82, $p < 0.001$) and that underweight was a protective factor.²³ In addition, compared with BMI and waist-to-height ratio (WtHR), WC had a

higher predictive value for HN (95% CI: 0.623-0.637, $p < 0.0001$), especially in males,³⁴ and the synergistic effect of WC and BMI was superior to a single index in identifying hypertension. The risk of HN increased in both gender among individuals who had the same WC with increasing BMI.²⁰ Being overweight has also been reported to increase the effect of ambient air pollution on HN.³⁵ However, the effect of neck circumference as an independent predictor of HN was not clear (OR=1.102, 95% CI=1.007-1.201, $p = 0.049$),³⁶ and it may be necessary to conduct a comparative study in a more representative group to elucidate the effect of this factor.

Pathological factors. Hyperuricemia is often reported to be independently associated with HN.³⁷ A multiple linear regression model in a substudy (n=60) demonstrated that only uric acid was a decisive factor in blood pressure, especially in males.³⁸ After standardizing the population by excluding people who were taking antihypertensive drugs, we found that people with high uric acid were more likely to present with HN (OR=1.50, 95% CI: 1.02-2.19).³⁹ The role of age in the relationship among insulin resistance, abnormal glucose tolerance, and HN is currently unclear. A study showed that impaired baseline fasting glucose (OR: 1.70, 95% CI: 1.07-2.69) was the strongest significant predictor of HN;⁴⁰ however, in another study, researchers found that the number of patients with HN was almost equal to those with normotension in the <52-year-old age group with insulin resistance, which may indicate that insulin resistance cannot be used as an independent predictor of HN in young adults.⁴¹ Therefore, the issues of whether there is an interaction between abnormal glucose tolerance and insulin resistance and whether it has a direct influence on HN progression in young adults deserve further discussion. Few studies have reported a link between immune factors and HN; one available study demonstrated that various inflammatory mediators, such as IgG, were involved in the nosogeny of HN through the mediation of anti-inflammatory and/or proinflammatory pathways⁴² in Chinese, Croatian, and Scottish populations.

Table 1 summarize the risk factors for prehypertension in young adults.

Unhealthy lifestyle. Elevated blood pressure has been shown to be related to some of unique lifestyles of young adults. A study developed to determine the effect of hikikomori (young adults who stay at home in long-term seclusion) on physical health showed that the SF-36 scores of this group were high, but the rates of

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Table 1 - Summary of risk factors for prehypertension (HN) in young adults.

Variable	Risk factors	Controversy
Obesity	Waist circumference, ³³ a combination of WC and BMI, abdominal obesity ³⁴	Neck circumference ³⁶
Pathological factors	Hyperuricemia, ^{37,39} impaired baseline fasting glucose, ⁴⁰ inflammatory mediators ⁴²	An interaction between abnormal glucose tolerance and insulin resistance ⁴¹
Lifestyle	Hikikomori, ⁴³ sleep less than 6 hours, ⁴⁴ decreased activity, ²⁹ tobacco use and heavy alcohol consumption ²³	
Diet	High in salt and fat, ⁴⁵ soft drinks, chocolate or candies 1-6 times a week ²³	
Social and psychological factors	Low life satisfaction, low social support and depressive symptoms, ²³ prenatal life stress events, ⁴⁶ the wealth gap, Lower education and a history of marital status ³¹	
Other factors	Wrist fracture, spina bifida, ⁴⁷ a serum FT4 level increase of 1 ng/dl ⁴⁹	A significant association between periodontal disease and hypertension instead of HN ⁴⁸

WC - waist circumference, BMI - body mass index, FT4 - free thyroxine,

HN remained as high as 31.7% and gradually increased in accordance with the concealment time,⁴² indicating that the lifestyle of “hikikomori” may be a related factor for obesity, cardiovascular disorders, and other chronic diseases among young adults. In addition, females aged 35-44 who slept less than 6 hours had an increased risk of HN (OR=1.769, 95% CI: 1.058-2.958).⁴⁴ Decreased activity,⁴⁴ tobacco use (OR=1.65, $p<0.01$) and alcohol use at least monthly (OR=1.96, 95% CI=1.32-2.54, $p<0.001$)²³ can also increase the risk of HN in young adults.

Unhealthy diet. Unhealthy diets, such as those high in salt and fat, have been identified as contributing factors to HN and hypertension in young adults. The average blood pressure of young adults who ate a high-salt diet was 130.40±7.20/86.10±4.05 mmHg, compared to 127.30±6.56/85.20±5.00 mmHg in prehypertensive young adults who ate a normal diet.⁴⁵ People who consumed more soft drinks (OR=1.56, $p<0.001$) and chocolates or candies 1-6 times a week (OR=0.73, $p<0.01$) were more likely to suffer from HN.²³ The relationship between other dietary factors and HN also deserves further investigation.

Social and psychological factors. In addition to physical changes, some psychological characteristics, such as low life satisfaction, low social support and depressive symptoms, have an impact on prehypertensive young adults.⁴⁶ Prenatal life stress events can affect the blood pressure of young adults (systolic blood pressure [SBP]: OR= -0.66, $p=0.013$ and diastolic blood pressure [DBP]: OR= -0.40, $p=0.047$).²³ In addition, the wealth gap also played an important role in predicting the incidence of HN, and the available evidence showed that

the rate of HN in rural areas was dramatically high in both the poorest (84.6%) and richest groups (28.1%).³¹ Lower education levels and marriage status were also related to the incidence of HN among inhabitants in Chongqing, China.¹⁸

Other factors. Prehypertension is one of the most common complications of hip fracture, and a positive relationship between wrist fracture and HN remains significant (OR = 1.48, 95% CI = 1.10-1.99).⁴⁷ However, whether other types of fracture are potential risk factors for HN is unclear. Young adults with spina bifida were more likely to suffer from HN compared with general individuals in the USA.⁴⁷ Although some studies reported positive correlations between periodontal disorders and HN, Kawabata found a significant relation between periodontal disorders and hypertension instead of HN after conducting a more rigorous prospective cohort study (OR: 0.93, $p=0.82$).⁴⁸ Additionally, a serum free thyroxine (FT4) level increase of 1 ng/dl was related to a 40% increase in risk of HN (OR=1.40, 95% CI=1.02 -1.90).⁴⁹

Prehypertensive intervention strategies. The 13th European Society of Hypertension in Milan in 2003 mentioned that patients should make active lifestyle changes, such as smoking cessation, weight control, salt restriction, and physical activity enhancement. Additionally, medication should be considered for patients who have more than 3 risk factors, and those patients who have diabetes mellitus and target organ damage should start drug treatment immediately if simple lifestyle changes cannot decrease blood pressure to below 130/80 mm Hg.

Prehypertension screening. Prehypertensive young adults may have milder clinical symptoms, making HN

more difficult to be diagnosed in young patients than in elderly patients. Therefore, in addition to effective interventions for diagnosed individuals, effective disease screening is necessary to improve prevention and awareness in potential HN patients. Both BMI and WC can be used to estimate the risk of HN,⁵⁰ and screening trials that focus attention on blood pressure and BMI can also help identify the related factors of cardiovascular disorders.¹⁴ Additionally, dynamic blood pressure monitoring,⁵¹ especially DBP monitoring,¹⁵ is conducive to the early recognition and administration of occult hypertension in young adults with HN.

Dietary intervention. Recent studies have suggested that there are some protective factors for HN, such as being a woman and highly educated, having a high household income and a healthy diet.¹⁵ Therefore, dietary interventions seem to be wise methods for preventing HN in young adults with high uric acid and those with smoking and alcohol consumption habits.³⁸ Foods with high salt and fat content have been recognized as dangerous risk factors for the development of HN. One study showed that the mean SBP was lower in young adults who consumed a low-salt diet than in young adults who consumed a high-salt diet (daytime 0.7 ± 5.8 mm Hg, $p=0.008$; night time 1.3 ± 6.1 mm Hg, $p<0.0001$).⁵² Juraschek found that moderate sodium intake (OR: -0.35 , $p=0.04$) and high sodium intake (OR: -0.33 , $p=0.003$) significantly reduced uric acid in all subjects compared to low sodium intake.⁵³ Functional foods are becoming popular with health-conscious citizens, as they offer a promising and effective nutritional strategy; for example, dietary polyphenols have shown potential benefits in the management of HN through the improvement and restoration of endothelial dysfunction and a decline in blood pressure.⁵⁴ In addition, a number of vegetables have high levels of nitrates, which can be reduced to nitrites by oral bacteria, undergo further reduction

to a kind of endogenous vasoprotective factor, nitric oxide (NO), and eventually indirectly achieve the goal of controlling blood pressure. For instance, a decline in SBP ($p<0.01$) and DBP ($p<0.001$) were closely associated with daily intake of beetroot juice, with water intake as the control, in a dose-dependent manner in young adults.⁵⁵

Lifestyle intervention. Comprehensive lifestyle changes, such as maintaining good sleep habits and increasing physical activity appropriately, are imperative because they can reduce the incidence of HN.¹ Aerobic exercise is regarded as the main form of exercise for young adults with HN because it has direct and continuous benefits on blood pressure and could decrease the blood pressure of prehypertensive patients by 5-7 mmHg on average.⁵⁶ A meta-analysis showed that exercise reduced SBP by 4.40 mmHg and DBP by 4.17 mm Hg in 3 months.⁵⁷ Furthermore, Sales et al⁵⁸ discovered that SBP in young women dropped from 128.2 ± 6.6 mm Hg to 118.0 ± 8.2 mm Hg ($p<0.05$) after a 12-week diet and exercise management program. Beck et al⁵⁹ also found that both resting SBP and DBP were similarly decreased in the HN groups after 8 weeks of resistance or endurance training. In addition, the difference in the changes in both SBP ($p<0.01$) and DBP ($p<0.01$) after an 8-week intervention between the Qigong group and the matched group were statistically significant.⁶⁰

Table 2 summarize the interventions for prehypertension in young adults.

Drug therapy. Drug treatment may be a cost-effective method to help stem the epidemic of HN in young adults who are currently free of CVD and may eventually reduce complications of HN. Julius et al⁶¹ and Luders et al⁶² suggested that the candesartan and angiotensin-converting enzyme inhibitor ramipril can reduce the risk of HN. Bhagatwala et al⁶³ found that there was a significant decline in peripheral SBP (-7.06 ± 2.25 mm Hg), peripheral

Table 2 - Summary of interventions for prehypertension in young adults.

Variable	Intervention strategies	Deficiency
Prehypertension screening	Screening trials focusing on blood pressure and body mass index, dynamic blood pressure monitoring ^{13,51}	
Dietary intervention	A low-salt diet, ⁵³ moderate sodium intake and high sodium intake, ⁵⁴ dietary polyphenols, ⁵⁵ beetroot juice ⁵⁶	Lack of comparison between different types of food or eating patterns
Lifestyle intervention	Aerobic exercise, ⁵⁷ resistance or endurance training, ^{59,60} Qigong ⁶¹	Current intervention strategies do not maintain long-term benefit
Drug therapy	Amiloride monotherapy, ⁶² allopurinol, ⁶³ acute dietary supplementation of a single dose of grape seed extract ⁶⁴	Lack of analysis of interactive effects between other interventions and prescription medication

DBP (-4.35 ± 1.67 mm Hg), central SBP (-7.68 ± 2.56 mm Hg), and central DBP (-4.49 ± 1.78 mm Hg) after 4 weeks of amiloride monotherapy. Fuchs et al⁶⁴ conducted a series of studies to explore the effectiveness of low-dose diuretic in adults with HN, and in 2016, they found that the combination of low-dose chlorthalidone and amiloride can effectively decrease the risk of hypertension and can benefit the left ventricular mass of patients, but their recent study indicated that a fixed association of chlorthalidone 12.5 mg and amiloride 2.5 mg didn't get most patients' blood pressure down to the ideal level.⁶⁵ Allopurinol can reduce the serum uric acid level ($p < 0.01$) and prevent the rise of 24-hours ambulatory DBP and daytime SBP and DBP.⁶⁶ Blood pressure can also be reduced in prehypertensive males by acute dietary supplementation of a single dose of grape seed extract.⁶⁷

Disease progression of prehypertension in young adults. Circulatory system damage. Prehypertension is closely related to CVD, and meta-analysis showed that HN dramatically increased the risk of CVD (relative risk (RR) 1.28, 95% CI 1.16-1.40), CHD ($p < 0.01$) and stroke mortality ($p < 0.01$), and the death of patients with CVD was largely driven by high-range HN (130-139 and/or 85-89 mmHg),⁶⁸ but even slightly elevated BP within the normal range is associated with cardiac end-organ damage.⁶⁹ Ennis et al⁷⁰ demonstrated that left ventricular structural damage (left ventricular mass in HN (31.26 ± 0.73 g/m (2.7), $p < 0.01$), diastolic function (the e'/a' ratio was 2.03 ± 0.06 in HN, which is lower than optimal, $p < 0.03$) and vascular dilation (aortic distensibility in HN (1.41 ± 0.05 mm Hg/cm (3)/m (2), $p < 0.01$) were impaired in prehypertensive youths, especially those with high-range HN.⁷⁰ In Markus' study, the HN group displayed more obvious aging-related increases of left ventricular wall thickness ($p < 0.001$) and left ventricular mass ($p = 0.006$), and HN was related to a raised incidence of left ventricular concentric remodeling (adjusted OR 10.7, 95% CI 2.82-40.4) and left ventricular hypertrophy (adjusted OR 5.33, 95% CI 1.58-17.9).⁸¹ Kurioka et al⁷² also suggested that both high-range and low-range HN were independent risk factors for CHD even in population aged 24-34 years.⁸ Thus, CVDs and cerebrovascular diseases, such as abdominal aortic aneurysms,⁷² CHD (RR=1.43, $p < 0.01$),¹⁰ intracranial arterial stenosis (ICAS) (OR=1.55, 95% CI=1.11-2.16, $p = 0.010$)¹¹ and stroke (RR=1.66, 95% CI=1.51-1.81), are associated with HN.⁷³

It is common for HN to progress to hypertension, and the 50th decade of life would be a critical period for this progression to occur.³³ A study in Japan showed that the relationship between baseline blood pressure and progressive blood pressure was stronger in the group aged 20-34 years than in the older age groups, especially in men.³³ Additionally, young adults with HN had a lower ankle-brachial index (ABI < 0.90 ; OR=3.288, 95% CI=1.5-7.0, $p = 0.0023$) and a higher incidence of peripheral artery disorders compared to the general population.⁷⁴

Endocrine system damage. The evidence for a link between HN and diabetes in young adults is limited, but the available evidence shows that baseline hypertension is a standalone predictive factor of incident diabetes mellitus (OR=3.33, $p < 0.01$). The serum retinol-binding protein 4 level was higher and independently related to SBP and DBP in prehypertensive Chinese young adults.⁷⁵ Moreover, recent evidence showed that an increase in serum aldosterone was correlated with HN in the general population.⁷⁶

Urinary system damage. Recent evidence showed that the prevalence of microalbuminuria was 6.8% in HN group and 3.6% in an optimal blood pressure group ($p < 0.001$).⁷⁷ A study suggested that HN had an all-important relationship with microalbuminuria (OR=2.50, $p < 0.05$) in the diabetes subgroup compared with the ideal blood pressure group,⁷⁸ indicating that there was an interaction between HN and diabetes mellitus, both of which may be predictors of slightly elevated albumin levels in urine. However, in another study, HN was more likely to be associated with slightly increased urinary albumin levels (OR=1.83, $p < 0.05$) after eliminating individuals with diabetes or hyperuricemia or those who used hypotensive drugs,³⁹ indicating that HN may be an independent predictor of microalbuminuria.

Subjects in the HN group had a mean B-type natriuretic peptide (BNP) level of 98 (72) pg/mL compared with 43.6 (20) pg/mL found among subjects in the normotension group ($p < 0.001$).⁷⁹ Bo found that the adjusted OR was 3.4 in the HN group and 1.6 in the control group in an attribution analysis of renal function injury;⁸⁰ both of these results suggest that persistent HN may be a standalone predictive factor of renal insufficiency. In addition to simple renal impairment, significantly higher numbers of simple renal cysts (SRCs) have been reported in young adults with HN and hypertension than in

those with normotension.¹³ Similarly, HN increased the risk of chronic kidney disease (CKD) (RR = 1.28, $p < 0.000$).⁸¹ The accumulated morbidity of CKD was higher in individuals with HN than in those in the general population (2.10% versus 1.46%, $p < 0.01$).⁸² In addition, a survey of 2.19 million young adults in the USA also indicated that prehypertensive patients had a 32% chance of advanced ESRF compared with individuals in the general population.¹²

Effects on pregnant women. Mild elevation of blood pressure during gestation can lead to high blood pressure or other diseases later in life. Studies have shown that after delivering a live infant, women with higher DBP levels (from 76.2±/-6.7 to 81.8±/-4.8 mm Hg) are more likely to suffer postpartum metabolic syndrome (OR=6.55, $P < 0.01$) than women with lower DBP levels.⁸³ HN in early pregnancy also had significant effects on total preeclampsia, early preeclampsia and severe preeclampsia (all $p < 0.05$).⁸⁴ In addition to the effect on pregnant women, HN is also related to both threatened premature labor and stillbirths.⁸⁵ Formulation of specific strategies for prehypertensive women in the child-bearing period has become a focus of research.

Other progressions in prehypertension. Autonomic dysfunction is both a cause and an effect of HN. Moinuddin found that there were 3 main changes in autonomic function in prehypertensive young adult males. First, sympathetic activity showed a significant increase among prehypertensive individuals characterized by a low increase in DBP (mmHg) in response to a hand-grip test (HGT) (11.27±/-3.76 mm Hg vs 23.95±6.29 mm Hg, [$p < 0.05$]). Second, the sympathovagal balance showed prominent sympathetic activity (2.85±1.78 versus 1.75±0.98; $p < 0.01$). Finally, parasympathetic activity was dramatically decreased.⁸⁶

In conclusion, HN continues to progress in young adults, but there are few rigorous randomized controlled trials to test the effectiveness, particularly the long-term utility, of exercise and lifestyle improvements. Further and practical research on young adults to construct a practical intervention model for prehypertension will be the focus of future research and will be significantly cost effective.

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