

Risk of Progression to Hypertension from Prehypertension and Normal Blood Pressure: Results from a Prospective Cohort Study among Industrial Workers in Kerala, India

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Abstract

Background: In India, studies exploring the incidence rate of hypertension (HTN) are limited particularly among industrial workers. We estimated the incidence rate of HTN among industrial workers with and without pre-HTN during a 2-year follow period and the factors associated with incident HTN among industrial workers in Kerala, India. **Materials and Methods:** A total of 326 industrial workers (mean age: 51 years, men: 76%), from two major industries in the state, enrolled at baseline were followed up at 2 years. All participants completed a structured interview schedule and had blood pressure (BP) and anthropometry measured using standard protocol. **Results:** Among the total workers, 36.5% were hypertensive, 39.3% were prehypertensive, and 24.2% had normal BP at baseline. At 2-year follow-up, 49.1% were hypertensive, 30.4% were prehypertensive, and 20.6% had normal BP. During follow-up, 19.8% of the 207 baseline nonhypertensives developed HTN providing an incidence rate of 9.9%/year (men: 10.7% and women: 7.6%). Incidence of HTN among ≥ 50 years was 11.4% compared to 9.0% among < 50 years. Among the 79 workers with normal BP at baseline, 31.6% progressed to pre-HTN and 13.9% developed HTN, and among the 128 prehypertensives, 23.4% developed HTN at year 2. The odds of progressing to HTN from pre-HTN was two times higher compared to those from normal BP. **Conclusion:** The findings of this study indicated a higher risk for prehypertensive to develop HTN. Efforts should be made to prevent or delay the progression to HTN focusing on prehypertensives with frequent follow-up.

Keywords: Incidence of hypertension, India, industrial workers, Kerala

INTRODUCTION

Hypertension (HTN), an important risk factor of cardiovascular morbidity and mortality, is the largest contributor to the global burden of diseases.^[1] Globally, during the past two decades, the number of hypertensives has doubled, and more than 19% of all deaths were related to high systolic blood pressure (SBP).^[2] Several studies found that pre-HTN increases the risk of developing HTN.^[3,4] People with pre-HTN are twice more likely to develop HTN compared to those with normal blood pressure (BP) as reported by the Framingham Heart Study.^[4] Considering the association of pre-HTN in the development of cardiovascular diseases, the Joint National Committee (JNC) VII criteria added pre-HTN as a new category.^[5,6] In a Jamaican cohort study, it was found that pre-HTN was associated with a threefold increase in HTN

incidence.^[7] A study among low-income Mexican population also reported a higher risk of progression to HTN among prehypertensives.^[8] The predictor role of pre-HTN with future HTN was also found in a cohort study among Korean adults.^[9] A population-based cohort study among Chinese adult women also reported that those with pre-HTN had a higher incidence of HTN compared to those with normal BP.^[10]

Globally, four in six people with HTN are living in low- and middle-income countries.^[11] HTN prevalence in India is

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on the rise which would soon become the “hypertension capital” of the world.^[12] There are different studies from India which reported HTN prevalence among adults^[13] and among industrial workers.^[14] However, follow-up studies on HTN which explored the progression rate of HTN among industrial workers are limited in India. The Indian state of Kerala was reported to have one of the highest rates of chronic diseases including HTN.^[15] However, limited information is available on the incidence of HTN in the state. A community-based study in Kerala reported an incidence rate of HTN as 24% during a 7-year follow-up period.^[16]

Our 2-year prospective study in Kerala estimated the incidence rate of HTN among people with and without pre-HTN at baseline and the factors associated with incident HTN among adult industrial workers.

MATERIALS AND METHODS

The study was conducted using data from a pilot study on the Community Interventions for Health (CIH). Methodology details and results from the adult community sample of CIH were published earlier.^[17] This was a community-based study conducted between 2008 and 2011 in three regions: Kerala state in India, Hangzhou city in China, and Mexico City in Mexico. In the present study, we analyzed BP among 326 workers who participated in the baseline and follow-up survey (mean age: 51 years, men: 76%).

Using the World Health Organization’s STEPS protocol for noncommunicable disease surveillance,^[18] we collected data on Step 1, Step 2, and Step 3. Demographic characteristics such as age and sex and behavioral characteristics such as tobacco use and alcohol consumption were collected. In Step 2, anthropometric risk factors such as weight, height, waist circumference, and BP were measured. In Step 3, blood samples were taken. We measured biochemical risk factors such as fasting plasma glucose (FPG), triglycerides (TGs), and high-density lipoprotein (HDL) cholesterol using Cholestech LDX system.^[19] BP was measured using Omron at baseline and at follow-up. A total of three readings with a gap of at least 5 min were taken, and the average of the last two readings was taken for analysis. Height was measured using stadiometer, weight using Seca weighing machine, and waist circumference using constant tension tape.

BP measurements were studied using the JNC VII criteria.^[5] Workers with SBP \geq 140 mmHg or diastolic BP (DBP) \geq 90 mmHg or on medication for HTN were considered to be hypertensive, SBP = 120–139 mmHg or DBP = 80–89 mmHg as prehypertensive, and SBP <120 mmHg and DBP <80 mmHg as normal. Controlled HTN was defined as SBP <140 mmHg and DBP <90 mmHg among hypertensive patients: Stage 1 HTN as SBP: 140–159 mmHg or DBP: 90–99 mmHg and Stage 2 HTN as SBP \geq 160 mmHg or DBP \geq 100 mmHg. Abdominal obesity was defined as waist circumference \geq 90 cm in males and \geq 80 cm in females. Diabetes was defined as FPG \geq 126 mg/dl or on medication for diabetes. Low HDL cholesterol

was defined as HDL cholesterol <40 mg/dl for men and <50 mg/dl for women or on medication for lipid abnormality, hypertriglyceridemia as TG \geq 150 mg/dl or on medication for lipid abnormality, hypercholesterolemia as total cholesterol \geq 200 mg/dl or on medication for lipid abnormality. Current tobacco users were defined as those who used any form of tobacco during the past 30 days. Current alcohol users were defined as those who consumed an alcoholic drink within the past 30 days.

Statistical analysis was done using IBM SPSS Statistics for Windows, version 21.0. (Armonk, NY: IBM Corp. Chicago, IL, USA). Chi-square test and Fisher’s test were used for comparison between categorical variables. The results are presented as unadjusted odds ratios (ORs) with 95% confidence intervals (CIs). The minimum statistical significance level was fixed as $P < 0.05$.

The study was approved by the Institute Ethics Committee of Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, Kerala, India. Written informed consent was obtained from all the participants before the study.

RESULTS

The baseline characteristics of the study participants are presented in Table 1. Among the 326 samples, 76% were men. The distribution of BP at baseline according to the JNC VII criteria is presented in Table 2. More than one-third of the participants, i.e., 36.5% (95% CI: 31.2–41.7), were hypertensive, 39.3% (95% CI: 34.0–44.6) were prehypertensive, and the remaining 24.2% had normal BP at baseline. Overall 20.2% of the hypertensives were under

Table 1: Baseline characteristics of the study participants (n=326)

Characteristics	n (%)
Age \geq 50 years	146 (44.8)
Men	246 (75.5)
Current tobacco users ^a	78 (23.9)
Current alcohol users ^b	118 (36.2)
BP	
Normal ^c	79 (24.2)
Pre-HTN ^d	128 (39.3)
HTN ^e	119 (36.5)
Abdominal obesity ^f	206 (63.2)
Diabetes ^g	85 (26.1)
Low HDL cholesterol ^h	216 (66.3)
Hypertriglyceridemia ⁱ	112 (34.4)
Hypercholesterolemia ^j	166 (50.9)

^aAny use of tobacco in the past 1 month, ^bAny alcohol use in the past 1 month, ^cSBP <120 and DBP <80, ^dSBP 120–139 or DBP 80–89, ^eSBP \geq 140 or DBP \geq 90 or on medication for HTN, ^fWaist circumference \geq 90 cm in males and \geq 80 cm in females, ^gFPG \geq 126 mg/dl or on medication for diabetes, ^hHDL cholesterol <40 mg/dl for men and <50 mg/dl for women, ⁱTG \geq 150 mg/dl, ^jTotal cholesterol \geq 200 mg/dl. HDL=High-density lipoprotein, BP=Blood pressure, SBP=Systolic BP, DBP=Diastolic BP, FPG=Fasting plasma glucose, TG=Triglyceride, HTN=Hypertension

Table 2: Distribution of blood pressure in the study sample according to the Joint National Committee VII stages by background characteristics

Variable	Nonthypertensives, n (%)		Hypertensives, n (%)		
	Normal BP ^a	Pre-HTN ^b	Controlled ^c	Stage 1 HTN ^d	Stage 2 HTN ^e
Total (n=326)	79 (24.2)	128 (39.3)	24 (7.4)	70 (21.4)	25 (7.7)
Men (n=248)	58 (23.4)	99 (39.9)	18 (7.3)	51 (20.6)	22 (8.9)
Women (n=78)	21 (26.9)	29 (37.2)	6 (7.7)	19 (24.4)	3 (3.8)
With diabetes mellitus ^f (n=85)	13 (15.3)	27 (31.8)	10 (11.8)	24 (28.2)	11 (12.9)
Abdominal obesity ^g (n=119)	21 (17.6)	44 (37.0)	11 (9.8)	32 (26.9)	11 (9.2)

^aSBP <120 and DBP <80, ^bSBP 120–139 or DBP 80–89, ^cSBP <140 and DBP <90 and on medication for HTN, ^dSBP 140–159 or DBP 90–99, ^eSBP ≥160 or DBP ≥100, ^fFPG ≥126 mg/dl or on medication for diabetes, ^gWaist circumference ≥90 cm in males and ≥85 cm in females. BP=Blood pressure, SBP=Systolic BP, DBP=Diastolic BP, FPG=Fasting plasma glucose, HTN=Hypertension

control of HTN (men: 19.8% and women: 21.4%). The control rate of HTN was slightly higher for those with diabetes. At the 2-year follow-up, 49.1% were hypertensive, 30.4% were prehypertensive, and 20.5% had normal BP. At year 2, 19.8% of the 207 workers who were either normal or prehypertensive at baseline developed HTN providing an incidence rate of 9.9%/year. Incidence of HTN among men was 10.7%/year compared to 7.6% among women ($P > 0.05$). Incidence of HTN among ≥50 years was 11.4% compared to 9.0% among <50 years ($P > 0.05$).

Table 3 gives the details of change in BP at 2-year follow-up according to baseline BP categories. Among the 79 workers with normal BP at baseline, 31.6% progressed to pre-HTN and 13.9% developed HTN, and among the 128 prehypertensives at baseline, 23.4% developed HTN at year 2. The odds of progressing to HTN from pre-HTN was close to two times higher compared to those from normal BP (OR: 1.89; 95% CI: 0.88–4.03).

Table 4 gives the bivariate analysis results of factors associated with incident HTN. Older participants (age ≥50 years) and men were more likely to progress from pre-HTN to HTN at year 2. Men and those with abdominal obesity, low HDL cholesterol, and diabetes were also more likely to progress from pre-HTN to HTN. Tobacco users were less likely to progress from pre-HTN to HTN compared to nonusers. However, alcohol users were more likely to progress from pre-HTN to HTN than nonusers of alcohol. The almost same pattern of association was seen in the progression from normal HTN at baseline to pre-HTN or HTN at year 2, except the finding that women and those with hypertriglyceridemia were likely to progress more from normal to pre-HTN or HTN at year 2 compared to their counterparts.

DISCUSSION

The finding of this study on the incidence of HTN is an illustration of the high risk of developing HTN in this population. Higher chance of HTN incidence among prehypertensive compared to normal BP has been reported in several follow-up studies.^[4,20] We also found comparable finding that pre-HTN doubles the risk of progression to HTN compared to people with normal BP. The higher progression in older age group was similar to that reported earlier.^[7] The

Table 3: Change in blood pressure category from baseline to 2-year follow-up (n=207)

Age and BP category at baseline	BP category at follow-up		
	Normal ^a	Pre-HTN ^b	HTN ^c
Age <50 years			
Normal BP (n=55)	33 (60.0)	13 (23.6)	9 (16.4)
Pre-HTN (n=73)	17 (23.3)	42 (57.5)	14 (19.2)
Age ≥50 years			
Normal BP (n=24)	10 (41.7)	12 (50.0)	2 (8.3)
Pre-HTN (n=55)	7 (12.7)	32 (58.2)	16 (29.1)
Total			
Normal BP (n=79)	43 (54.4)	25 (31.6)	11 (13.9)
Pre-HTN (n=128)	24 (18.8)	74 (57.8)	30 (23.4)

^aSBP <120 and DBP <80, ^bSBP 120–139 or DBP 80–89, ^cSBP ≥140 and DBP ≥90 and on medication for HTN. BP=Blood pressure, SBP=Systolic BP, DBP=Diastolic BP, HTN=Hypertension

above study found that women were more likely to progress to HTN from pre-HTN compared to their men counterparts, which is contrary to our finding that men were more likely to progress to HTN from pre-HTN compared to women. This might be due to the smaller proportion of women in our sample.

A long-term Framingham Heart Study (26-year follow-up) reported that the development of HTN was two times higher for those with high normal BP.^[21] Even though several studies reported the uncertainty of the association between alcohol use and HTN,^[22,23] our study found higher odds of progression to HTN among alcohol users. Similar to earlier findings,^[24] obesity was found to be a major risk factor for development and progression to HTN in the present study. Reported studies on tobacco use and HTN showed inconsistent findings. Some studies reported that smokers have lower BP than nonsmokers,^[25,26] whereas the role of tobacco use in increasing HTN has been well established.^[27]

The effect of risk factors on the progression from pre-HTN to HTN did not reach statistical significance. This may be due to the short follow-up period of 2 years in our study and the small sample size of the cohort. Pharmacological treatment of pre-HTN was found to be more effective in decreasing the onset of HTN compared to nontreatment group.^[28] The study participants were industrial employees who can be considered

Table 4: Factors associated with incident hypertension results of bivariate analysis

Baseline characteristics	Progression to HTN (n=128) (pre-HTN to HTN)		Progression to HTN or pre-HTN (n=79) (normal to pre-HTN or HTN)	
	Percentage	Unadjusted OR (95% CI)	Percentage	Unadjusted OR (95% CI)
Age (years)				
<50	19.2	Reference	40.0	Reference
≥50	29.1	1.72 (0.75-3.93)	58.3	2.10 (0.79-5.56)
Sex				
Women	17.2	Reference	47.6	Reference
Men	25.3	1.62 (0.55-4.70)	44.8	0.89 (0.32-2.43)
Abdominal obesity ^a				
No	20.2	Reference	44.8	Reference
Yes	29.5	1.65 (0.71-3.82)	47.6	1.11 (0.41-3.04)
Low HDL cholesterol ^b				
No	22.5	Reference	37.9	Reference
Yes	23.9	1.08 (0.44-2.62)	50.0	1.63 (0.64-4.15)
Hypertriglyceridemia ^c				
No	25.0	Reference	43.3	Reference
Yes	20.5	0.77 (0.31-1.86)	52.6	1.45 (0.51-4.09)
Hypercholesterolemia ^d				
No	30.5	Reference	48.8	Reference
Yes	17.4	0.48 (0.20-1.10)	42.1	0.76 (0.31-1.85)
Diabetes ^e				
No	20.8	Reference	45.5	Reference
Yes	33.3	1.90 (0.74-4.84)	46.2	1.02 (0.31-3.39)
Current tobacco use ^f				
No	26.0	Reference	46.8	Reference
Yes	14.3	0.47 (0.15-1.49)	41.2	0.79 (0.26-2.36)
Current alcohol use ^g				
No	22.0	Reference	42.0	Reference
Yes	27.0	1.31 (0.54-3.16)	51.7	1.48 (0.59-3.71)

^aWaist circumference ≥90 cm for men and ≥80 cm for women, ^bHDL cholesterol <40 mg/dl for men and <50 mg/dl for women, ^cTG ≥150 mg/dl, ^dTotal cholesterol ≥200 mg/dl, ^eFPG ≥126 mg/dl or on medication for diabetes, ^fAny use of tobacco in the past 1 month, ^gAny alcohol use in the past 1 month. HDL=High-density lipoprotein, TG=Triglyceride, FPG=Fasting plasma glucose, HTN=Hypertension, OR=Odds ratio, CI=Confidence interval

as belonging to middle-income categories who might be healthier, which might affect the generalization of the study finding to the general population.

CONCLUSION

Our study indicated a higher chance of prehypertensive to develop HTN even though a considerable proportion of people with normal HTN at baseline developed HTN at 2-year follow-up independent of other risk factors (albeit not statistically significant). Further investigation of pharmacological treatment for prehypertensive for delaying the onset of HTN in the future needs to be explored further in this population. However, considering the cost of pharmacological treatment for HTN, efforts should be made to prevent or delay the progression to HTN focusing on prehypertensive with frequent follow-up as well as the interventions to reduce other risk factors identified in this study.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Forouzanfar MH, Liu P, Roth GA, Ng M, Biryukov S, Marczak L, *et al.* Global burden of hypertension and systolic blood pressure of at least 110 to 115 mm hg, 1990-2015. *JAMA* 2017;317:165-82.
- Institute of Health Metrics and Evaluation. Elevated Blood Pressure is the Top Risk for Health Loss Worldwide. Institute of Health Metrics and Evaluation; 2017. Available from: <http://www.healthdata.org/announcement/elevated-blood-pressure-top-risk-health-loss-worldwide>. [Last retrieved on 2019 Jul 15].
- Harvard Men's Health Watch. Prehypertension: Does it Really Matter? Available from: <https://www.health.harvard.edu/heart-health/prehypertension-does-it-really-matter>. [Last retrieved on 2019 Jun 19].
- Vasan RS, Larson MG, Leip EP, Kannel WB, Levy D. Assessment

- of frequency of progression to hypertension in non-hypertensive participants in the Framingham heart study: A cohort study. *Lancet* 2001;358:1682-6.
5. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, *et al.* The seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure: The JNC 7 report. *JAMA* 2003;289:2560-72.
 6. Lenfant C, Chobanian AV, Jones DW, Roccella EJ. Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Seventh report of the Joint National Committee on the prevention, detection, evaluation, and treatment of high blood pressure (JNC 7): Resetting the hypertension sails. *Hypertension* 2003;41:1178-9.
 7. Ferguson TS, Younger N, Tulloch-Reid MK, Lawrence-Wright MB, Forrester TE, Cooper RS, *et al.* Progression from prehypertension to hypertension in a Jamaican cohort: Incident hypertension and its predictors. *West Indian Med J* 2010;59:486-93.
 8. Jimenez-Corona A, Lopez-Ridaura R, Stern MP, Gonzalez-Villalpando C. Risk of progression to hypertension in a low-income Mexican population with prehypertension and normal blood pressure. *Am J Hypertens* 2007;20:929-36.
 9. Kim SJ, Lee J, Nam CM, Jee SH, Park IS, Lee KJ, *et al.* Progression rate from new-onset pre-hypertension to hypertension in Korean adults. *Circ J* 2011;75:135-40.
 10. Sun Z, Zheng L, Detrano R, Zhang X, Xu C, Li J, *et al.* Risk of progression to hypertension in a rural Chinese women population with prehypertension and normal blood pressure. *Am J Hypertens* 2010;23:627-32.
 11. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in blood pressure from 1975 to 2015: A pooled analysis of 1479 population-based measurement studies with 19.1 million participants. *Lancet* 2017;389:37-55.
 12. Joshi SR, Parikh RM. India – Diabetes capital of the world: Now heading towards hypertension. *J Assoc Physicians India* 2007;55:323-4.
 13. Zachariah MG, Thankappan KR, Alex SC, Sarma PS, Vasana RS. Prevalence, correlates, awareness, treatment, and control of hypertension in a middle-aged urban population in Kerala. *Indian Heart J* 2003;55:245-51.
 14. Jeemon P, Prabhakaran D, Goenka S, Ramakrishnan L, Padmanabhan S, Huffman M, *et al.* Impact of comprehensive cardiovascular risk reduction programme on risk factor clustering associated with elevated blood pressure in an Indian industrial population. *Indian J Med Res* 2012;135:485-93.
 15. Thankappan KR, Shah B, Mathur P, Sarma PS, Srinivas G, Mini GK, *et al.* Risk factor profile for chronic non-communicable diseases: Results of a community-based study in Kerala, India. *Indian J Med Res* 2010;131:53-63.
 16. Sathish T, Kannan S, Sarma PS, Razum O, Thankappan KR. Incidence of hypertension and its risk factors in rural Kerala, India: A community-based cohort study. *Public Health* 2012;126:25-32.
 17. O'Connor Duffany K, Finegood DT, Matthews D, McKee M, Narayan KM, Puska P, *et al.* Community interventions for health: A novel approach to tackling the worldwide epidemic of chronic diseases. *CVD Prev Control* 2011;6:47-56.
 18. Surveillance of Risk Factors for Non Communicable Diseases. The WHO STEP wise Approach. Non Communicable Diseases and Mental Health. Geneva: World Health Organization; 2003. Available from: http://www.who.int/ncd_surveillance/steps/riskfactor/en/index.html. [Last retrieved on 2019 Mar 10].
 19. Carey M, Markham C, Gaffney P, Boran C, Maher V. Validation of a point of care lipid analyser using a hospital based reference laboratory. *Ir J Med Sci* 2006;175:30-5.
 20. Winegarden CR. From “prehypertension” to hypertension? Additional evidence. *Ann Epidemiol* 2005;15:720-5.
 21. Leitschuh M, Cupples LA, Kannel W, Gagnon D, Chobanian A. High-normal blood pressure progression to hypertension in the Framingham heart study. *Hypertension* 1991;17:22-7.
 22. Fuchs FD, Chambless LE, Whelton PK, Nieto FJ, Heiss G. Alcohol consumption and the incidence of hypertension: The atherosclerosis risk in communities study. *Hypertension* 2001;37:1242-50.
 23. Stranges S, Wu T, Dorn JM, Freudenheim JL, Muti P, Farinano E, *et al.* Relationship of alcohol drinking pattern to risk of hypertension: A population-based study. *Hypertension* 2004;44:813-9.
 24. Zhao G, Ford ES, Li C, Mokdad AH. Weight control behaviors in overweight/obese U.S. Adults with diagnosed hypertension and diabetes. *Cardiovasc Diabetol* 2009;8:13.
 25. Li G, Wang H, Wang K, Wang W, Dong F, Qian Y, *et al.* The association between smoking and blood pressure in men: A cross-sectional study. *BMC Public Health* 2017;17:797.
 26. Okubo Y, Suwazono Y, Kobayashi E, Nogawa K. An association between smoking habits and blood pressure in normotensive Japanese men: A 5-year follow-up study. *Drug Alcohol Depend* 2004;73:167-74.
 27. Halperin RO, Gaziano JM, Sesso HD. Smoking and the risk of incident hypertension in middle-aged and older men. *Am J Hypertens* 2008;21:148-52.
 28. Julius S, Nesbitt SD, Egan BM, Weber MA, Michelson EL, Kaciroti N, *et al.* Feasibility of treating prehypertension with an angiotensin-receptor blocker. *N Engl J Med* 2006;354:1685-97.