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Original Article

Risk factors in pre-hypertensive individuals for cardiovascular morbidity. a population based study in wardha district of central india.

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ABSTRACT

Aim: To assess the association between prehypertension and risk factors for cardiovascular disease.Material and Methods: The study was carried out in Acharya Vinoba Bhave Rural Hospital (AVBRH)/DMIMS University and JN Medical college of Wardha District in the year 2011. AVBRH is a 950 bedded rural hospital. 200 persons (100 controls and 100 cases p;rehypertensives) between 35–75 years old, completed a questionnaire and had anthropometric and blood pressure measurements performed using standardized procedures. Fasting glucose was measured using a capillary blood sample. Analysis yielded crude, and sex-specific estimates for prehypertension and other Cardiovascular Diseases(CVD) risk factors. Odds ratios for associations of prehypertension with CVD risk factors were obtained using Logistic Regression. Observations and Results: Prehypertension was more common in males, 35% (CI 31%–39%), than females, 25% (CI 22%–28%). Almost 46% of participants were overweight; 19.7% were obese; 7.2% had diabetes mellitus and 17.8% smoked cigarettes. With the exception of cigarette smoking and low physical activity, all the CVD risk factors had significantly higher prevalence in the prehypertensive group (p for trend < 0.001) compared to the normotensive group. Odds of obesity, overweight, and increased waist circumference were significantly higher among younger prehypertensive participants (35–54 years old) when compared to normotensive young participants, but not among those 55–75 years-old. Among men, being prehypertensive increased the odds of having >/=3 CVD risk factors versus no risk factors almost three-fold (odds ratio [OR] 2.8 [CI 1.1–7.2]) while among women the odds of >/=3 CVD risk factors was increased two-fold (OR 2.0 [CI 1.3–3.8]). Conclusion: Prehypertension is associated with increased prevalence of other CVD risk factors. Health-care providers should recognize the increased CVD risk of prehypertension and should seek to identify and treat modifiable risk factors in these persons. It is time that we prescribe healthy lifestyle and help patients "fill the lifestyle prescription".

1. Introduction

India has been successful in reducing a bunch of communicable diseases. However, rapid cultural changes and social advances have led to the manifestation of wide range of non-communicable diseases. A high prevalence of diabetes, obesity, hypertension and metabolic syndrome exists in the country today.

Hypertension affects nearly 26 per cent of the adult population worldwide[1]. Hypertension is an important independent predictor of cardiovascular disease, cerebrovascular accidents and death [2-4]. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-7) defines hypertension as blood pressure >140/90 mmHg.

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Persons with blood pressure above optimal levels, but not clinical hypertension (systolic blood pressure of 120-139 mm Hg or diastolic blood pressure of 80-89 mm Hg), are defined as having "pre- hypertension" [5]. Persons with pre-hypertension have a greater risk of developing hypertension than do those with lower blood pressure levels [5]. In addition, pre-hypertension is associated with increased risk of major cardiovascular events . This new classification places a large number of persons previously considered as normal in this higher risk category and emphasizes the need for monitoring and possible intervention in people with blood pressures between the range of normal and hypertensive.

The prevalence of cardiovascular diseases and hypertension is rapidly increasing in developing countries . This increase, which was previously most marked in the urban population, is now seen even in the rural setting. It is likely to be related to changing life-styles and to an increased longevity. Cardiovascular diseases are estimated to have led to 1.59 million deaths in India in the year 2000 and this figure is projected to increase to 2.03 million for the year 2015[6]. Hypertension has been reported to be responsible for 57 per cent of all stroke deaths and 24 per cent of all cardiovascular deaths in East Asians .

The prevalence of pre-hypertension has increased over time . Pre-hypertension progresses to clinical hypertension at a rate of 19% over 4 years [6]. Pre-hypertension is a risk factor for overt hypertension, and since the publication of the JNC-7 report, several studies have assessed the prevalence and significance of pre-hypertension but little is known about the risk factors associated with it.

Aim And Objectives

The aim of this study is to assess the association between prehypertension and some known risk factors for coronary artery and cardiovascular disease such as:

(i) Weight

(ii) Body Mass Index

(iii) Waist Circumference

(iv) Waist-Hip Ratio

(v) Diabetes Mellitus/ Impaired Glucose Tolerance

(vi) Cigarette Smoking

(vii)Low physical activity

Material and Methods

A representative village in Wardha district was chosen and Cross-sectional study for duration of 6 months was done using Simple Random Sampling technique.

Assuming a prevalence of pre-hypertension equal to 20 per cent, a sample size of 200 was calculated to give the true prevalence with a precision of 2 per cent with 95 per cent of confidence level.

Selection criteria for cases :

(I) Inclusion Criteria: - Only adults above 35 years of age.

- People who have given informed consent.

(ii) Exclusion Criteria:

· All people suffering from previously diagnosed hypertension or under the drug treatment for the same.

· Pregnant women.

· People suffering any renal disorders.

· Disabled and acutely ill people.

Controls:

· People between age group of 35– 75 years

· People with no family history of hypertension.

· People with no diagnosed pre-hypertension or hypertension.

· People with no history of chronic diseases.

· People with no active illness (as per clinical and paraclinical data).

Data collection :

All eligible subjects were selected from the medicine wards and OPD (random blood sugar levels were taken as frequent visits from the patients was a flaw) For each subject, a detailed history was taken followed by anthropometric measurements.

1. Blood Pressure Measurement:

Blood pressure has been measured as the systolic blood pressure (SBP) / diastolic blood pressure (DBP)

Example: 120/ 80 where 120 is the SBP and 80 is the DBP.

The following precautions were taken while measuring the blood pressure:

(i) The BP was measured after the patient has been seated for 10 minutes to adjust to the temperature in the examining room and no less than 1 hour after exercising, smoking, or consuming tea/ coffee.

(ii) The participant's arm was placed at the heart level in both seated position and standing position in both the arms.

(iii) Two measurements were taken. If the difference between the 2 measurements was greater than

10 mm Hg, a third measurement was taken. SBP was defined as the average of the closest 2 SBP readings. DBP was defined as the average of the closest 2 DBP readings.

(iv) A cuff of proper size was used in accordance with the official guidelines.

Blood pressure has been categorized as:

BLOOD PRESSURE	MEAN SBP (in mm Hg)	MEAN DBP (in mm Hg)
Normal	<120	<80
Pre-hypertensive	120-139	80-89
Hypertension 1	140-159	95-99
Hypertension 2	> 160	>100
Isolated Systemic Hypertension	> 140	< 90

2. Weight:

It was measured (to the nearest kg) with the subject standing motionless on the weighing scale, and with the weight distributed equally on each leg.

3. Body Mass Index:

It is an assessment of body weight relative to height. This has been calculated in the following way:

BMI= Weight (in kilograms)

Height (in metres) 2

Height was measured using a Harpendon stadiometer while weight was recorded using a weighing machine (Avery India Ltd.) with beam balance (sensitivity of scales up to 100 g).

Height was measured with the subject standing in an erect position against a vertical scale and with the head positioned in the Frankfurt Plane.

The BMI has been expressed as follows:

BMI < 18.5: Underweight
BMI = 18.5 – 25: Normal weight
BMI = 25-30: Overweight
BMI = 30-35: Obesity class I
BMI = 35-40: Obesity class II
BMI > 40: Obesity class III

4. Waist Circumference:

5. Waist Hip Ratio (WHR):

Waist circumference was measured at the midpoint between lowermost point of the costal margin and highest point of iliac crest with the subject standing, at the end of normal expiration. Hip circumference was measured at the level of the greater trochanters with the subject wearing minimum clothes.

WHR = Waist Circumference

Hip Circumference

The cut-off used to define obesity for both males and females was 0.9.

6. Blood Glucose (By glucose oxidase-peroxidase technique):

All subjects, except those known to have diabetes, underwent an oral glucose tolerance test in accordance with World Health Organization guidelines. Blood samples (10 mL) were collected with sterile technique using disposable syringes. Samples for plasma glucose were collected in fluoride vials, was separated within half an hour in the field itself. All samples were transported on ice to the laboratory in our institute. Plasma glucose was measured by the glucose oxidase-peroxidase technique.

Subjects were considered hyperglycemic if their fasting blood glucose level was >126 mg/dL.

7. Cigarette Smoking:

The reported number of cigarettes smoked per day was recorded, and subjects were defined as smokers if they smoked >1 cigarette per day.

8. Physical Activity:

Sedentary lifestyle was defined by the routine performance of <1 physical activity per week.

Statistical analysis

Statistical analyses were performed using SPSS Statistical Package Version 16. Continuous variables were expressed as mean ± standard deviation. Categorical variables were presented as frequencies. Risk factors for normo-tension and pre-hypertension have been separately tested in a univariate logistic regression analysis. Variables have been age and sex adjusted. For the purpose of regression analysis variables have been categorized into units as follows:

Age: 10 years,

BMI: >5 kg/m2,

All variables which were significant in univariate analysis were then tested by multiple logistic regression analysis A two-tailed P value <0.05 will be considered significant.

The Chi-Square statistic corrected for survey design determined evidence of statistically significant association between cardiovascular risk factors and blood pressure categories. Multivariate Logistic Regression analysis provided estimates of the odds of prehypertensive participants having given risk factors as well as various clusters of risk factors. Separate models were created for each cardiovascular risk factor. Each model estimated the relative increase in the odds of having the respective risk factor for prehypertensive persons compared with normotensive persons. To examine the clustering of risk factors for cardiovascular disease, we estimated the proportion of participants within blood pressure categories having one, two or three or more of the five aforementioned additional risk factors. We then used logistic regression models to calculate sex-specific, age adjusted odds ratios for having one, two, or three or more additional risk factors among prehypertensive participants compared to those with normal blood pressure.

Table 1: Means and standard deviation for characteristics within and across normotensive and pre-hypertensive categories

Characteristic	Total (n= 200)	Normotension (n=100)	Pre-hypertension (n=100)	p Value for association*
Age (Years)	36.3 + 0.45	30.3 + 0.44	36.6 + 0.73	<0.001
Weight (kg)	71.5 + 0.47	67.5 + 0.55	74.0 + 0.75	<0.001
Height (cm)	167.1 + 0.33	166.6 + 0.39	168.6 + 0.56	0.002
Body Mass Index (kg/m^2)	25.7 + 0.18	24.4 + 0.22	26.1 + 0.28	<0.001
Waist circumference (cm)	82.3 + 0.41	77.9 + 0.48	84.1 + 0.64	<0.001
Hip circumference (cm)	99.7 + 0.46	97.1 + 0.53	101.3 + 0.62	<0.001
Waist-Hip Ratio	0.82 + 0.003	0.82 + 0.003	0.83 + 0.003	<0.001
Fasting Blood Glucose	4.3 + 0.05	4.0 + 0.04	4.21 + 0.07	<0.001

Values are shown as Mean + SD

Apart from height, all characteristics showed a statistically significant increasing trend ($p < 0.001$) going from normotensive to pre-hypertensive

Table 2: Crude and sex-specific prevalence of cardiovascular disease risk factors

Characteristic	Males (n= 100) % (95% CI)	Females (n=100) % (95% CI)	Total (n=200) % (95% CI)
Obesity (BMI > 30 kg/m2)	9.0 (6.8-11.3)	30.0 (26.8-33.2)	19.7 (17.4-22.0)
Overweight (BMI > 25 kg/m2)	30.2 (25.7-34.6)	60.7 (57.4-64.0)	45.7 (42.6-48.9)
Increased Waist Circumference(cm)	14.6 (11.6-17.6)	56.7 (53.2-60.2)	36.0 (33.0- 39.0)
Increased Waist- Hip Ratio	6.1 (4.0-8.1)	54.4 (50.6-58.2)	30.5 (27.9-33.2)
Diabetes Mellitus/ Impaired Glucose Tolerance	26.3 (24.3-28.3)	28.0 (26.6-29.4)	27.2 (26.0-28.3)
Cigarette Smoking**	28.3 (24.1-32.5)	0.0	28.3 (24.1-32.5)
Low Physical Activity	21.3 (17.3-25.4)	50.9 (46.8-54.9)	36.3 (33.0-39.7)

**** Currently smokes cigarettes regardless of quantity per day**

*** p < 0.001 (male – female difference in proportions)**

Table 3: Prevalence of individual cardiovascular risk factors and risk factor clusters by sex and blood pressure categories

Individual cardiovascular risk factor	Males % (95% CI)			Females % (95% CI)		
	Normal BP	Pre-HTN	p Value	Normal BP	Pre-HTN	p Value
Obesity (BMI > 30 kg/m2)	4.8(2.0–7.5)	8.6(4.9–12.4)	< 0.001	19.7(16.6–22.8)	39.0(32.7-45.2)	< 0.001
Overweight (BMI > 25 kg/m2)	19.2(14.4–24.0)	31.2(24.9–37.5)	< 0.001	48.4(44.1–52.8)	71.3(65.8-76.9)	< 0.001
Increased Waist Circumference(cm)	6.3(3.2–9.4)	13.7(8.7–18.6)	< 0.001	42.4(37.9–46.8)	66.9(60.8-72.9)	< 0.001
Increased Waist- Hip Ratio	2.6(0.4–4.9)	4.7(2.0–7.6)	< 0.001	42.1(37.2–47.0)	60.4(54.6-66.2)	< 0.001
Diabetes Mellitus/ Impaired Glucose Tolerance	2.2(0.6–3.8)	4.3(1.9–6.6)	0.004	2.4(1.3–3.5)	7.2(4.8–9.5)	0.033
Cigarette Smoking**	31.7(24.6–38.8)	28.8(21.6–35.9)	0.007	8.0(5.7–10.3)	6.8(3.7–10.0)	0.181
Low Physical Activity	18.7(13.1–24.3)	20.8(14.1–27.4)		52.0(47.2–56.9)	46.2(39.8-52.7)	
Risk factor clustering	**Males % (95% CI)**			**Females % (95% CI)**		
	Normal BP	**Pre-HTN**	**p Value**	**Normal BP**	**Pre-HTN**	**p Value**
No additional risk factor	54.1(47.9–60.3)	45.6(37.1–54.1)	< 0.001	48.4(43.9–52.8)	22.6(16.2-29.2)	< 0.001
1 additional risk factor	33.1(26.5–39.6)	28.0(21.9–34.1)	0.225	33.6(29.3–37.9)	40.9(35.3-46.5)	< 0.001
2 additional risk factor	11.0(6.8–15.2)	19.6(13.6–25.5)	< 0.001	13.8(10.9–16.7)	25.8(20.5-31.2)	< 0.001
>3 additional risk factor	1.8(0.4–3.2)	6.8(3.5–10.2)	< 0.001	4.2(2.4–6.1)	10.6(7.6–13.5)	< 0.001

Table 4: Age specific odds ratios (with 95% CI in brackets) from multivariate logistic regression models for cardiovascular disease risk factors among prehypertensive persons compared to normotensive persons

Risk factor	35-44 years	45-54 years	55-64 years	>65 years
Obesity (BMI > 30 kg/m^2)	2.8 (1.8–4.3)	1.8 (0.8–3.9)	1.1 (0.5–2.5)	0.9(0.2–3.5)
Overweight (BMI > 25 kg/m^2)	1.4 (0.9–2.3)	1.3 (0.6–2.8)	1.0 (0.4–2.6)	1.1(0.3–3.5)
Diabetes Mellitus/ Impaired Glucose Tolerance	0.7 (0.2–2.7)	1.8 (0.7–5.0)	2.4 (0.8-7.9)	4.1(0.8–19.8)
Increased Waist Circumference(cm)	1.4 (0.9–2.2)	1.6 (0.8–3.3)	1.6 (0.5–4.7)	1.6(0.4–5.7)
Increased Waist- Hip Ratio	1.03 (0.6–1.8)	3.1 (1.3–7.3)	1.0 (0.5-2.2)	0.8(0.3–2.8)

Central obesity was present in 96 per cent of males and 77 per cent of females surveyed. Among the cardiovascular In the study population, the prevalence of overweight and obese subjects was 47 and 32 per cent respectively risk factors, serum LDL cholesterol was elevated in 23 per cent, 43 per cent of males were current or ex-smokers and 47 per cent had abnormal glucose tolerance (IGT 17%, diabetes mellitus 25%). The age and sex adjusted prevalence of was significantly higher in males (36%) compared to females (28.1%; P<0.0001). The prevalence of prehypertension in the youngest age group was 36 per cent. Its prevalence either did not change (in females) or was lower with increasing age (in males, P< 0.05) In the age group 35-44 yr, 50 per cent of subjects were normotensive, while among those in the age groups >65 yr only 14 per cent had normal blood pressure.

As a group, subjects with either pre-hypertension or hypertension had increased body mass index, waist-hip ratio and higher prevalence of IGT/diabetes compared to those with normal blood pressure. Of the four risk factors for cardiovascular disease (central obesity, LDL cholesterol,IGT /diabetes and smoking), two or more were present in 49, 63 and 66 per cent of males (P<0.05) and in 32, 47 and 66 per cent of females (P<0.0001) with normal blood pressure, pre-hypertension and hypertension respectively. As compared to normotensive subjects, being overweight/obese increased odds pre-hypertension (OR 1.6, P=0.007). Similarly, central obesity was associated with increased odds of having prehypertension (OR 2.0, P=0.001).

5. Discussion

Our study documents the association of prehypertension and cardiovascular risk factors in a rural population. Analysis of the NHANES III data set has provided similar results. The prevalence of pre-hypertension was significantly higher in males compared with females. Pre-hypertensive subjects had greater obesity, central abdominal obesity and had an increased prevalence of diabetes/IGT compared to normotensive subjects. The same risk factors were further increased in subjects with hypertension. This finding was in concordance with studies on pre-hypertension from developed market economies. Greenlund [7] reported that subjects with pre-hypertension were 1.65 times as likely to have at least 1 other adverse cardiovascular risk factor than those who were normotensive and to have 1.8 times increased risk of cardiovascular events. Obesity and sedentary lifestyle are important modifiable risk factors for hypertension. In the current study, being overweight or obese increased the odds of having pre-hypertension by 1.6 times respectively. Among subjects who were centrally obese, nearly and 30 per cent were pre-hypertensive. Central obesity increased the odds of pre-hypertension even among subjects who had a normal BMI. Previous studies have emphasized the propensity of Indians to develop central obesity and insulin resistance. We also found an increased risk of prehypertension among subjects with sedentary lifestyle, though this was not confirmed on multivariate analysis. Similar results have been shown in different ethnic groups including Indians.

On multivariate analysis, increasing age, BMI, waist-hip ratio and the presence of diabetes or IGT independently contributed to pre-hypertension.

Thus, endothelial dysfunction and a generalized inflammatory state, coupled with a high prevalence of CVD risk factors, together provide a likely explanation for the increased rate of CVD events among prehypertensive subjects. It is well established that hypertension should be controlled and, when possible, prevented. Some question remains, however, as to the appropriate therapeutic approach to prehypertension. Over the last decade, attention has been drawn to the diagnosis and treatment of disease during the preclinical stages, before the progression to overt clinical manifestations.

The true question regarding prehypertension is not the mere method of its progression to overt hypertension but rather the global CVD risk associated with this condition and the potential risk reduction to be gained by early initiation of treatment. A simulation model has shown that elimination of prehypertension results in a substantial public health benefit, thus providing the rationale for an interventional approach to this condition. It is important to note that prehypertension, per se, is not associated with an increased risk of CVD, unless accompanied by additional risk factors. However, only 10% of prehypertensive subjects have this condition alone. Accordingly, subjects with prehypertension are at risk for CVD events, and a global risk reduction is indicated. Current guidelines recommend lifestyle modifications alone, because no studies have evaluated the efficacy of pharmacological interventions on prehypertension.

Our study had certain limitations. Subjects for the study were chosen from a single locality and thus may not be representative of rural population throughout India. However, we took care to choose a village which had a representative mix of subjects with all different professions, age groups and religions.

This represents a great societal cost with major loss of life expectancy and quality of life. Recent studies have demonstrated that individuals in prediabetic state can be identified and diabetes can be delayed if not prevented [8]. Similarly, the pre-hypertension category is designed to focus physicians, patients and public attention on blood pressure (BP) in the 120–139 mm Hg systolic and/or 80– 89 mm Hg diastolic range with the aim to slow down or prevent the progression of rising blood pressure, arterial stiffness and kidney damage that occurs over time.

6. Conclusion

Our study demonstrates that prehypertension is associated with multiple cardiovascular risk factors. (as cardiovascular morbidity is emerging as a leading cause of sickness)These results further underline the need for routine BP measurements in young adults to identify subjects with prehypertension who should be the target of lifestyle modification. We believe that the increased prevalence of obesity and sedentary lifestyle observed today would make behavioral changes the most logical and effective choice for modifying the natural history of prehypertension and its progression to overt hypertension and increasing a healthy lifestyle to reduce chances of cardiovascular sickness.

Further studies should be designed to assess the role of prehypertension(playing an important indicator towards identifying risk factors and a early initiative for clinicians for halting or reducing the progress of disease) as an independent cardiovascular risk factor and to assess the effect of lifestyle modification and therapeutic interventions on the progression to hypertension, as well as on cardiovascular morbidity and mortality.

Lifestyle modifications without drug therapy are recommended for all patients with prehypertension to effectively reduce cardiovascular risk. Obesity and diabetes are important modifiable risk factors for hypertension. It is time that the doctors consider joining with others in the community to find out what in the community helps or works against healthy lifestyles. There are pervasive disincentives to healthy exercise and incentives to unhealthy diet built into the very structure of our towns, cities and economy. When we prescribe drugs, we know (usually) that our patients can fill the prescription. What about when we prescribe healthy lifestyle? We can help our patients “fill the lifestyle prescription” by becoming involved in such issues as fast-food outlets in schools, provision of safe walking/jogging in parks, or exercise facilities in workplaces. This challenge is one that we can all

take up, as members of and leaders in our communities. Lastly, and perhaps most importantly, we need to know what really works for prehypertension. What sorts of interventions that are feasible to carry out in the clinician's office make a difference in lifestyle and reduce prehypertension? How can we best arrange our office workflow and systems to deliver lifestyle interventions effectively? What are patients' goals? How does prehypertension fit into the care of the whole patient? How is it balanced against patients' other health care and broader life stage needs? What side effects (positive or negative) does prehypertension management have? Outcome studies are needed to establish the value of pharmacologic therapy for the treatment of prehypertension.

7. References

[1] World Health Report 2002. Reducing Risks, Promoting Healthy Life. Geneva, Switzerland: World Health Organization, 2002.

[2] Chobanian AV, Bakris GL, Black HR, 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.

[3] Wang Y, Wang QJ. The prevalence of prehypertension and hypertension among U.S. adults according to the new joint national committee guidelines: new challenges of the old problem. Arch Intern Med 2004;164:2126 –34.

[4] Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet 2002;360:1903–13.

[5] Qureshi AI, Suri MF, Kirmani JF, Divani AA, Mohammad Y. Is prehypertension a risk factor for cardiovascular diseases? Stroke 2005;

[6] 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: 1682–1686.

[7] Geenlund KJ, Croft JB, Mensah AG. Prevalence of Heart Disease and Stroke Risk factors in Persons with Prehypertension in United States. Arch Intern Med. 2004;164(19):2113-8.

[8] Perreault L, Pan Q, Malhar KJ, Watson KE, Hamman RF, Kahn SE. Effect of regression from Prediabetes to normal glucose regulation on long term reduction in diabetes risk: results from the Diabetes Prevention Program Outcomes Study. The Lancet. 2012;379(9833):2243-51.`