Rate and Risk of All Cause Mortality among People with Known Hypertension in a Rural Community of Southern Kerala, India: The Results from the Prolife Cohort

Anu Kuriakose[1,2], Thekkumkara Surendran Nair Anish[2], Biju Soman[1], Ron Thomas Varghese[1], Thekkumkara Prabhakaran Sreelal[2], Alice Matilda Mendez[2], Anitha Abraham[2]

[1]Health Action by People (HAP), Thiruvananthapuram, Kerala, India,, [2]Department of Community Medicine, Government Medical College, Thiruvananthapuram, Kerala, India

Correspondence to:
Dr. Thekkumkara Surendran Nair Anish, Department of Community Medicine, Government Medical College, Thiruvananthapuram, Kerala - 695 011, India.
E-mail: doctrinets@gmail.com

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Original Article

ABSTRACT

Background: Hypertension is one of the most important determinants of death due to vascular damage and is fast emerging as a high burden disease in India. However, its documentation is poor in the country. This study aims to estimate the rate and the causal pattern of mortality in a cohort of people with high blood pressure as compared to normotensives.

Methods: The study setting is Varkkala, a rural village in southern Kerala, India, and the study design was that of a prospective cohort. A total of 77,881 participants of age 20 years and above were considered for analysis. The rate and risk of all cause mortality (death due to any cause) among hypertensives were quantified and compared against the normotensives. The causes of death were also analyzedin both the groups. Cox proportional hazard models were created to estimate the hazard ratios of death among hypertensives adjusted for sociodemographic factors, behaviors, and comorbidities.

Results: The incidence proportion of deaths in the study was 4.28% during the follow-up period of 6 years. The relative risk of mortality was 3.13 (CI: 2.91-3.37) in the high BP group. The age-adjusted hazard ratio of all cause mortality for the high BP group was 2.96 (2.56-3.42). Coronary artery disease was the major cause of death among the subjects with high BP.

Conclusions: The study revealed high prevalence of hypertension in the study population. A person with hypertension is at three times higher risk of death due to any cause compared to a normotensive individual even after adjustment for age.

Keywords: All cause mortality, hypertension, hypertension and death, hypertension in Kerala

INTRODUCTION

Systemic hypertension has emerged as one of the primary risk factors for heart disease and stroke, the leading causes of death worldwide.Hypertension is estimated to victimize more than 1.56 billion by the year 2025.[1] It has reached epidemic proportions with nearly one fourth of the global adult population suffering from it.[1] It remains undetected for long periods in a significant proportion of patients. Indian studies have shown that most of the 'hypertensives' in the community are unaware of their blood pressure (BP) status and among those aware only 5-10% are adequately treated; this complicates the problem at hand.[2,3]

The risk of death due to high BP is more than double in low and middle-income countries.[1] Primary hypertension is the direct causative factor for 57% of all stroke deaths and 24% of all coronary heart disease deaths in India.[4,5] This is complicated by the fact that most of the cardiovascular events appear early in Indian ethnic group compared to the Western counterparts.[6] It is the need of the hour to devise sustainable strategies in order to retard the emerging epidemic of cardiovascular events like coronary heart diseases and stroke, in India. Thus prevention and management of hypertension is one of the most important strategies that should be adopted to reduce these cardiovascular events.

Kerala, the leading state in India with respect to health indicators, is undergoing an epidemiological change with a rise in the elderly population and a significantly high morbidity and mortality due to chronic diseases.[7,8] Several studies have documented the absolute and relative burden of hypertension in Kerala and the rates are one of the highest in India.[9,10] But there are not many studies which have documented the stake of hypertension on mortality among the Indian population. This made us embark on this study to estimate the rate and causal pattern of mortality in a cohort of people with high BP, in a rural village in Kerala, India.

METHODS

The study has used the data of 'PROLIFE' (Population Registry of Lifestyle Diseases), a prospective long-term cohort study following up rural residents of Varkkala community development block in Thiruvananthapuram district, South Kerala.[11] The community development block comprised the jurisdiction of seven local self-governments known as GramaPanchayaths. The data was collected by a non-profit-oriented public health research organization, Health Action by People (HAP). A detailed household survey was carried out between 1 July and 31 December 2001. All the households in the area were identified (n = 34 190) and the baseline and follow-up data were collected by health workers trained in data collection techniques and data management. From 1 July 2002, the households were visited regularly at three monthly intervals and the vital events were reported in a predesigned format. As of 31 December 2004, 0.01% of the population moved out of the study area and was lost to follow-up. The database included the details of all residents who were 20 years of age and above, during the baseline data collection. No sampling was done as the entire cohort of eligible participants was considered for analysis. The eligibility criterion for inclusion in the analysis was age more than or equal to 20 years at the time of baseline survey. No residents (residing in the study area at least for 6 months) were excluded from the cohort. The data on other family members, if unavailable in the house even at the second visit of the preliminary data collection was collected from the relatives, preferably the head of the family. Enumeration of events was started from 1July 2002 and the follow-up time for the analysis was 6 years (31 June 2008). The participation rate was 97.6%. The sociodemographic variables of the subjects, habits of tobacco, and alcohol consumption, healthy practices like regular physical activity and the details on deaths were considered in this study. The details of the data collection of the cohort have been documented elsewhere.[11]

The primary outcome variable was mortality (death due to any cause) to and the status of physician diagnosed hypertension as was reported by them during the baseline survey was the major exposure variable. Time to event (death) was taken as the outcome variable to build Cox-proportional hazard models. Effect of confounding due to other sociodemographic variables like age, gender, socioeconomic status, behaviors like physical activity, smoking, alcoholism and comorbidities like diabetes mellitus, pre-existing heart diseases, and other chronic diseases were evaluated. The physical activity was calculated as the sum of work time and leisure time physical activity, each of which was measured on a 3-point scale and the subjects were classified into high and low physical activity groups using the median value as a cut-off. The smoking status was classified as ever or never smokers based on any history of smoking in the past. The diabetic status was obtained from history of physician diagnosed disease and with the help of laboratory results. The socioeconomic status was classified as high and low with respect to the median value of the monthly income of the subjects.

Statistical analysis

Continuous variables were represented using mean with standard deviation and categorical variables as frequencies and percentages. The incidence proportion of deaths was calculated for the subjects with high BP and those with normal BP, at the end of follow-up. The relative risk of death among the known hypertensive group was calculated and this relative effect measure was adjusted for various factors which interact between high BP and all cause death. Cox proportional hazard models were created to estimate the hazard ratios of death among people diagnosed as having hypertension compared to normotensives adjusted for sociodemographic factors, behaviors, and comorbidities. The statistical analysis was done using SPSS version 16.

Ethical considerations

A written informed consent was obtained from the head of the family of each household. Community consent was obtained from the democratic leader of the Panchayath. The study was granted approval by the ethical committee of HAP.

RESULTS

The study population ($n = 77881$) was constituted by 44,142 women (56.7%). The median (IQR) age was 39 (28, 53) years. A history of having physician diagnosed high BP was reported by 10.4% of the study participants. The median (IQR) age of the subjects with high BP was 57 (47, 66) years. The proportion of subjects with high BP in the 20-29 age category was 1.12% and it increased to 26.94% in the 60 years and above age category [Table 1]. Among women, high BP was reported by 12% while it was 8.2% among men. In the high socioeconomic stratum, high BP was reported by 12.54% of the subjects and it was 10.8% among those who studied up to a secondary school level. A history of pre-existing heart disease was given by 4% of the subjects and diabetes mellitus was previously diagnosed in 6.9%, by laboratory tests. The sociodemographic characteristics of the study population and the proportion of subjects with high BP across the various categories are shown in Table 1. Among the total subjects, 44.5% were from a low socioeconomic status and 90.6% had studied up to higher secondary school level. A high level of physical activity was practised by 38.8% of them. Among the total subjects, 79.1% never smoked.

The incidence proportion of deaths in the study was 4.28% during the 6 year follow-up period. Among the people with high BP, the incidence proportion of deaths was 11%; while it was 3.5% among those with a normal BP. The relative risk of mortality was 3.13 (2.91, 3.37) indicating an all cause mortality risk three times higher among people with high BP as compared to those with a normal BP.

The relation between all cause mortality among people with high BP and those with a normal BP across different variables is shown in Table 2. In the 20-29 year age group, the risk of mortality was 3.1-times greater among subjects with high BP than those with a normal BP. However, in the high BP group, with advancing age, the relative risk was decreased to 1.2 in the 60 years and above-age category, although the mortality was greater, indicating age as a major interacting variable. Women with high BP experienced a 1.5-times greater risk of mortality than their corresponding male counterparts. High BP was found to contribute to higher death rates cutting across all demographic, socioeconomic, and comorbidity categories [Table 2].

The total number of deaths among the subjects with high BP was 890. The causes of death across the various age categories are shown in Table 3. The number of deaths was highest in the 60 years and above age category (80%). Coronary artery disease accounted for the largest (34%) single cause of death in that age category followed by cerebrovascular disease (CVD) and chronic obstructive pulmonary disease. The incidence proportion of deaths due to ischemic heart diseases (IHD), CVD, diabetic complications and kidney diseases was greater among the high BP group across all the age categories [Table 4]. But the difference in the

Table 1: The sociodemographic characteristics of the study population and proportion of subjects with high BP

Variables	Categories	Proportion of subjects in percentage 100% (*n*=77,881)	Proportion of subjects with high BP 10.37% (*n*=8074)	*P* value*
Age (years)	20-29	27 (21063)	1.2 (236)	<0.001**
	30-39	24 (18663)	4.0 (754)	
	40-49	18.4 (14337)	10.3 (1477)	
	50-59	12.9 (10066)	19.0 (1912)	
	60 and above	17.7 (13752)	26.9 (3695)	
Gender	Women	56.7 (44142)	12.0 (5311)	<0.001
	Men	43.3 (33739)	8.2 (2763)	
Education	Up to pre degree	90.6 (68299)	11.2 (7665)	<0.001
	At least a degree	9.4 (7068)	5.8 (409)	
Socioeconomic status	Low	44.5 (33063)	8.2 (2707)	<0.001
	High	55.5 (41159)	13.0 (5367)	
Physical activity	Low	57.5 (44782)	12.1 (5423)	<0.001
	High	42.5 (33099)	8.0 (2651)	
Smoking	Ever smoker	20.9 (16277)	10.7 (1747)	0.122
	Never smoker	79.1 (61604)	10.4 (6327)	
Pre-existing heart disease	Present	4 (3115)	40.4 (1255)	<0.001
	Absent	96 (74766)	9.2 (6819)	
Diabetic status	Diabetic	6.9 (5374)	46.1 (2470)	<0.001
	Non-diabetic	93.1 (72507)	7.9 (5604)	

*Chi-square test unless specified otherwise; **Chi-square for trend; BP=Blood pressure

Table 2: Risk of death across various covariate categories stratified for hypertension

Variables	Categories	Incidence of death		Relative risk in each category (CI)
		High BP group (*n*=890) (%)	Normal BP group (*n*=2451) (%)	
Age	20-29	4 (1.68)	113 (0.54)	3.11 (1.16-8.36)
	30-39	13 (1.71)	169 (0.94)	1.82 (1.04-3.19)
	40-49	36 (2.43)	242 (1.88)	1.29 (0.91-1.82)
	50-59	121 (6.30)	329 (4.03)	1.56 (1.28-1.91)
	60 and above	716 (19.32)	1598 (15.9)	1.21 (1.12-1.31)
Gender	Women	463 (8.71)	1020 (1.1)	3.31 (2.98-3.68)
	Men	427 (15.47)	1431 (4.62)	3.34 (3.02-3.70)
Socioeconomic status	Low SES	299 (11.48)	1168 (3.83)	3.00 (2.66-3.38)
	High SES	578 (11.19)	1233 (3.42)	3.27 (2.97-3.59)
Education	Up to pre-degree	824 (11.16)	2237 (3.67)	3.04 (2.82-3.28)
	Degree and above	22 (5.58)	71 (1.06)	5.25 (3.29-8.38)
Physical activity	Low (*n*=40,771)	566 (11.6)	1352 (3.76)	3.08 (2.82-3.28)
	High (*n*=30,218)	198 (8.29)	788 (2.83)	2.92 (2.52-3.4)
Smoking	Ever smokers (16,267)	252 (17.35)	935 (6.29)	2.76 (2.43-3.14)
	Never smokers (61,488)	638 (9.59)	1516 (2.76)	3.48 (3.19-3.81)
Pre-existing heart disease	Present (*n*=3082)	218 (17.31)	223 (12.17)	1.42 (1.2-1.69)
	Absent (*n*=74,673)	672 (9.82)	2228 (3.27)	3.00 (2.76-3.26)
Diabetic status	Diabetic (*n*=5396)	401 (16.18)	332 (11.37)	32.89 (28.6-37.82)
	Not diabetic (*n*=72,485)	489 (8.69)	2119 (3.16)	2.75 (2.5-3.02)

BP=Blood pressure, SES=Socioeconomic status, CI= Confidence interval

Table 3: Adjusted hazard ratios for different models

Regression models	Covariates adjusted for	Hazard ratio (95%CI)	*P* value
Model 1	Unadjusted	3.27 (3.03, 3.53)	<0.001
Model 2	Adjusted for age, age*hypertension (age is an interacting variable)	2.96 (2.56, 3.42)	<0.001
Model 3	Adjusted for demographic (age, age*hypertension and gender), socioeconomic status, education, and physical exercise	2.94 (2.51, 3.43)	<0.001
Model 4	Adjusted for demographic (age, age*hypertension and gender), socioeconomic status, education, physical exercise, smoking, diabetic status and pre-existing heart disease	2.40 (2.05, 2.82)	<0.001

Table 4: The causes of death and the death rates per thousand among the high BP and normal BP subjects across age categories

Causes of death	Incidence of death as events per 1000 individuals among high BP		Incidence of death as events per 1000 individuals among normal BP	
	<60 years (*n*=4392)	>60 years (*n*=3706)	<60 years (*n*=59737)	60 years (*n*=10046)
Coronary artery diseases	15.7 (69)	66.1 (245)	4 (239)	40.9 (411)
Cerebrovascular diseases	6.3 (28)	35.6 (132)	0.6 (37)	20.1 (202)
Chronic obstructive pulmonary diseases	0.9 (4)	28.8 (107)	0.7 (44)	36.3 (365)
Attributed to diabetes mellitus	3.4 (15)	14.5 (54)	0.6 (40)	6.1 (62)
Cancers	5.2 (23)	12.1 (45)	2.1 (124)	13.0 (131)
Injuries	2.9 (13)	4.8 (18)	3.4 (205)	6.9 (70)
Renal disease	2.9 (13)	4.8 (18)	0.5 (30)	2.8 (29)
Infections	1.1 (5)	6.2 (23)	1.2 (70)	7.6 (77)
Attributed to old age	-	16.7 (62)	-	23.3 (234)
Miscellaneous	0.9 (4)	4.5 (17)	1.0 (60)	6.4 (65)
Total	39.6 (174)	194.5 (721)	14.2 (849)	163.8 (1646)

BP=Blood pressure

rates across the two groups was more marked below 60 years of age. The incidence of IHD was five times and that of CVD 10 times higher among young (below 60 years) 'hypertensives' as compared to their non-hypertensive counterparts.

Survival analysis was done for the two groups of subjects with high and normal BP. The difference in survival observed between the groups was significant by log-rank test ($P < 0.001$). But it was evident that factors like sociodemographic variables and comorbidities could modify the mortality rates in relation to hypertension. The unadjusted hazard ratio of all cause mortality among those with high BP was as high as 3.27 (3.03, 3.53). The high rate ratio could be due to the fact that the subjects with high BP were significantly older than the general population. Age was found to be an interacting variable between hypertension and all cause mortality. The variable 'age' was dichotomized and was multiplied with the variable 'hypertension status' to create a new variable to measure the interaction. The age-adjusted hazard ratio for all cause mortality among hypertensives was 2.96 (2.56 -3.42). The hazard ratio among people aged more than 60 years adjusted for hypertension was 10.84 (10.02, 11.72). The hazard ratio for age-hypertension interaction was 0.82 (0.70-0.96). Two other models were also created by adjusting for other sociodemographic variables, behaviors, and comorbidities, the findings of which are given in Table 3. High BP was found to be a risk factor for early death in all the models.

The burden of hypertension and its complications increase with age. Age was found to be an interacting variable in the present data on mortality among hypertensives. When subjects with normal BP aged less than 60 years was the referent group with hazard ratio for mortality 1, the high BP subjects with age less than 60 years had a hazard ratio of 2.96; while the subjects with high BP and older than 60 years had a hazard ratio of 14.14 for mortality.

DISCUSSION

In the study, it was seen that more than 10% of the subjects knew their hypertensive status; the actual proportion of those with high BP would have been much higher. This finding was consistent with the higher rates of hypertension reported in Kerala.[9] This could be due to the epidemiological transition as a result of the emergence of risk factors[10] and to the increased awareness about this non-communicable disease in the local community. A retrospective population survey in North America involving 26 million people conducted around the same time period, have documented a self-reported hypertension prevalence rate of almost 23% in the same age category as this study.[12]

The higher risk of cardiovascular diseases and all cause mortality among those with high BP have been documented widely in different ethnic groups and communities.[13-17] But a quantification of the risk is important in each setting to initiate public health activities suited to and relevant in that setting. There may be differences in the mechanisms by which hypertension contributes to mortality which may be unique to each source population. Even a large cohort study conducted in America failed to prove the common belief that hypertension contributes significantly to stroke.[13] But such an association does exist in estimates from the eastern part of the world.[4,5] This study has also documented CVDs as one of the leading causes of death among 'hypertensives' next only to IHDs.

The death rate of subjects with high BP in this study was found to be three times more than their counterparts with normal BP. The multivariate models suggested that a considerable amount of this difference could be attributed to the fact that 'hypertensives' in the present study were significantly older than the 'normotensives'. In addition, comorbidities like diabetes mellitus and behaviors like smoking also contributed to the higher death rates among people with high BP. Evidence has shown that diabetes mellitus and smoking increases the mortality risk among hypertensives.[14] It should be noted that the all cause mortality rates among the high BP group remained high even after adjusting for all demographic, socioeconomic, behavioral, and other comorbid factors.

Even though the greater death rate among individuals with high BP is often predicted by the extent of target organ damage,[18] the end-stage vascular injuries in hypertension can be delayed by adherence to pharmacotherapy[19-21] and lifestyle modifications.[21-25] The measures of social wellbeing like higher educational status may impart healthy choices in living conditions and lifestyle of individuals which in turn can prevent the complications in hypertensives as has been noticed in the present study. This finding is consistent with the available documented evidence.[22] Physical exercise was found to be protective for all cause mortality among people with high BP. There is ample evidence that cardiorespiratory fitness, decreased adiposity, and muscle strength protect morbid individuals from death.[23-27] The lack of opportunities for girls and women for physical exercise make them more vulnerable for cardiovascular diseases like hypertension.[28] Comorbidities like diabetes mellitus make the arena more complicated. Diabetes mellitus has a synergistic effect with hypertension on the mortality.[29] The burden of diabetes mellitus is found to be higher in the population of Kerala compared to other rural Indian settings.[30]

CONCLUSIONS

Kerala is often considered as one of the socially developed states of India with life expectancy and mortality rates comparable to developed nations of the world. However, the morbidity rates of chronic diseases like that of hypertension are also high in the state. The current study throws light in to the quantification of the mortality burden which is attributed directly by hypertension in the community. It also explains the relationship between high BP and death in the presence of social and behavioral factors and other comorbidities. This study points to the rising mortality burden associated with a chronic non-communicable disease like hypertension in developing countries.

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