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Original Article

Isolated diastolic hypertension and its risk factors in semi-rural population of South India

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ABSTRACT

Background: Isolated diastolic hypertension (IDH) has been actively discussed for the last two decades because of its prevalence in a younger population and its association with cardiovascular disease. Furthermore, the association of IDH is significant in South Asian Countries such as India because relatively younger populations are known to have a higher risk of cardiovascular events.
Objective: The objective of this study is to find prevalence of IDH and its risk correlates in a semiurban population of South Indian state of Andhra Pradesh.
Methods: Data were collected using the modified World Health Organization - STEPwise approach to Surveillance (WHO STEPS) questionnaire for 16,636 individuals from a group of villages under Thavanampalle Mandal. Collated data were analyzed for prevalence and risk factors of IDH.
Results: Prevalence of IDH was found to be 4.0% with mean age of 46.0 (±SD 13.6) years and a relatively higher prevalence in men (5.3%) as compared with women (3.2%). The prevalence of IDH peaked in the fifth decade of life (40–49 years of age) and declined thereafter. Among various risk factors that were analyzed for their association with IDH, only age, body weight, and body mass index retained their significance in multivariate binary logistic regression analysis.
Conclusion: There is a significant prevalence of IDH below 50 years of age in the semiurban population of South India. As IDH in young and middle age is known to be associated with increased risk of cardiovascular events and end organ involvement, it highlights need for study and development of effective IDH management strategies to reduce associated morbidity and mortality.

1. Introduction

Hypertension is one of the most important preventable causes of cardiovascular disease.[1] Furthermore, prevalence of hypertension continues to rise in developing countries such as India.[2] As per the JNC-7 classification, hypertension is defined as systolic blood pressure (SBP) ≥ 140 mm of Hg or diastolic blood pressure (DBP) ≥ 90 mm of Hg[3] and has been further divided into 3 categories: (a) isolated diastolic hypertension (IDH; SBP < 140 mm of Hg and DBP ≥ 90 mm of Hg), (b) isolated systolic hypertension (ISH; SBP ≥ 140 mm of Hg and DBP < 90 mm of Hg), and (c) systolic–diastolic hypertension (SDH; SBP ≥ 140 mm of Hg and DBP ≥ 90 mm of Hg).[4] While ISH and SDH are very well associated with cardiovascular diseases (CVD) including stroke, coronary artery disease, and heart failure, association of IDH has been found to be a better predictor of CVD only among those less than 50 years of age.[5] In South Asian countries including India, events of acute myocardial infarction occur at a younger age (53.0 ± 11.4 years) as compared with Western countries (58.8 ± 12.2 years).[6] Therefore, it is important to identify prevalence of IDH and important risk factors that predispose to IDH so that effective management protocols may be formulated specifically for South Asian countries.

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2. Material and methods

2.1. Selection of subjects

The study was approved by Apollo Health Education and Research Foundation, Apollo Hospitals, Jubilee Hills, Hyderabad. A door-to-door survey was conducted using the modified World Health Organization - STEPwise approach to Surveillance (WHO STEPS) questionnaire at Thavanampalle Mandal, one of the 66 mandals in Chittoor district in the South Indian state of Andhra Pradesh, covered under 'Total Health', a Corporate Social Responsibility arm of Apollo Hospitals Enterprises Ltd. Everyone older than 15 years who consented to participate were included in the study. Informed consent was obtained from all subjects included in the study in a language they understood (Telugu/Kannadiga), and their signature/thumb imprint was obtained. Those who did not provide their consent were excluded from the study.

2.2. Study design and sample size

This was a population study in which prevalence of isolated diastolic hypertension was unknown. Minimum sample size for a population with unknown prevalence is calculated using the following formula:

$$Z^2 \ X\, p(1-p) \Big/ C^2$$

where Z is Z-score or confidence level (taken as 99% or Z-score of 2.576), p is standard deviation (taken as 0.5), and C is confidence interval (margin of error) (taken as ±1%)

With the aforementioned formula, a sample size of 16,589 would provide a confidence level of 99% with standard deviation of 0.5 and confidence interval as ±1%.

Furthermore, a total of 15 variables have been analyzed for their association with IDH using univariate and multivariate logistic regression models. Because 10 events per variable (EPV) have been found to be good enough for logistic regression analysis,[7] our sample size of 16,636 had enough EPV for the analysis.

2.3. Data collection

Data were collated and analyzed for 16,636 individuals (62.3% females and 37.7% males) whose blood pressure was recorded. These individuals were part of 8947 families with an average number of 1.86 members from each family (median 2). Trained healthcare workers keyed in the data in android tablets using application software specifically developed for this survey. Three consecutive recordings were made for every BP measurement using automatic oscillometric BP measurement devices, and an average of these three values was used for the data analysis. Random capillary blood glucose was measured using glucometer (AccuChekPerforma). Quality assurance measures included training of data collectors, supervision of a proportion of visits and measurements by researchers, and periodic calibration of BP instruments. Calibration of glucometers was carried out every month by randomly matching 2% of the blood glucose level result with the laboratory at the local Apollo hospital and every week by comparing with another glucometer. Results that were within 15% of the laboratory reading were considered accurate. Body weight was measured using a digital weighing scale, and anthropometric measurements were carried out using a measuring tape. Other variables were subjective responses of the subjects to the modified WHO STEPS questionnaire. The number of EPV has been recorded in Table 2, and any missing variables were excluded in both univariate and multivariate logistic regression analysis.

A database was created in MySQL and analyzed using SPSS 16 and MS Excel. More details on methods have also been published elsewhere.[2] The Kolmogorov–Smirnov test was used as test of normality. Statistical analysis of independent categorical variables with dependent continuous data was carried out using binary logistic regression technique of SPSS. Univariate and multivariate regression models were utilized for risk factor analysis. Further details of model have been provided in results section. Sample size for each risk factor categorical variable has been given in Column 2 (N) of Table 2, and individuals with missing data were excluded in the models of risk factor analysis.

3. Results

Prevalence, mean age, and sex preponderance of IDH, ISH, and overall hypertension (as per JNC-7 classification) in study population has been tabulated in Table 1. IDH had a prevalence of 4% in the surveyed population with a male preponderance (males 5.3% cf. females 3.2%) and a mean age of 46.0 (SD ± 13.6). ISH had a prevalence of 9.7% with a mean age of 60.8 (SD ± 15.3) and with almost equal distribution among the two sexes (male 10.5% and females 9.2%). Mean DBP (±SD) and SBP (±SD) of the surveyed population was 76.5 (±12.1) mm of Hg and 123.8 (±19.5) mm of Hg, respectively. As shown in Table 1, mean SBP of those with IDH was more than the mean DBP and SBP of the surveyed population.

As shown in Fig. 1, the prevalence of IDH was higher in 30–49 years of age group with highest being in the age group of 40–49 years. IDH at age <50 years is considered a risk factor for cardiovascular disease, and around 61.5% (411) of those with IDH were less than 50 years of age in the study group. While IDH starts declining at 50 years of age, ISH is seen to rise almost exponentially after this age.

Various risk factors for hypertension were analyzed for association with IDH. On univariate binary logistic regression analysis by SPSS, risk factors including male gender, rising age, marital status, employment status, income per month, body mass index, body weight, cooking oil consumed, alcohol consumption, family history of diabetes, and family history of hypertension showed significant association on Wald Chi-squared test as shown in Table 2.

However, on multivariate binary logistic regression analysis by SPSS, only the associations with age, Body Mass Index (BMI), and body weight remained significant. Odds of IDH were 2.20 [95% confidence interval (CI): 1.44–3.35] among individuals between 25 and 39 years of age, 2.84 (95% CI; 1.84–4.37) among individuals between 40 and 59 years of age, and 1.94 (95% CI: 1.22–3.07) among individuals greater than 60 years of age as compared with individuals with less than 25 years of age. Odds of IDH were 1.87

Table 1
Prevalence, mean age of individuals, sex preponderance, mean SBP (±SD) of individuals, and mean DBP (±SD) of individuals among those classified as isolated diastolic hypertension (IDH), isolated systolic hypertension (ISH), and hypertension (as per JNC-7 classification) in the study population.

Hypertension Sub-type	Prevalence (%)	Mean age (±SD)	% among male population	% among female population	Odds ratio (male/female)	Mean SBP (±SD)	Mean DBP (±SD)
Isolated Diastolic Hypertension (n = 668)	4.0	46.0 (±13.6)	5.3%	3.2%	1.68 (1.44–1.96)	129.8 (±8.4)	93.8 (±5.5)
Isolated Systolic Hypertension (n = 1616)	9.7	60.8 (±15.3)	10.5%	9.2%	1.16 (1.04–1.29)	152.4 (±12.6)	79.4 (±7.7)
Hypertension (n = 3594)	21.6	56.2 (±15.4)	25.6%	19.2%	1.44 (1.34–1.56)	150.8 (±17.0)	89.4 (±12.3)

Table 2
Univariate and multivariate binary logistic regression analysis for risk factor analysis of isolated diastolic hypertension.

Risk Factor		N	Univariate logistic regression		Multivariate logistic regression	
			Odds ratio (95% CI)	Wald Chi-squared value (p-value)	Odds ratio (95% CI)	Wald Chi-squared value (p-value)
Gender	Male	6276 (37.7%)	1 (base)		1 (base)	
	Female	10360 (62.3%)	**0.59 (0.51–0.69)**	**42.7 (<0.001)**	0.78 (0.58–1.05)	2.66 (0.103)
Age	<25 years	2326 (14.0%)	1 (base)		1 (base)	
	25–39 years	4295 (25.8%)	**3.16 (2.18–4.60)**	**36.50 (<0.001)**	**2.20 (1.44–3.35)**	**13.38 (<0.001)**
	40–59 years	5558 (33.4%)	**4.09 (2.85–5.88)**	**58.08 (<0.001)**	**2.84 (1.84–4.37)**	**22.21 (<0.001)**
	> = 60 years	4457 (26.8%)	**2.24 (1.53–3.28)**	**16.98 (<0.001)**	**1.94 (1.22–3.07)**	**7.88 (<0.005)**
Education	>=Graduate	1804 (10.8%)	1 (base)		1 (base)	
	ITI/Sr Sec	1965 (11.8%)	1.02 (0.74–1.39)	0.01 (0.925)	1.17 (0.84–1.64)	0.86 (0.353)
	Primary-middle school	6813 (41.0%)	1.14 (0.89–1.48)	1.05 (0.306)	1.12 (0.84–1.50)	0.61 (0.436)
	Illiterate	6054 (36.4%)	0.71 (0.54–0.93)	6.31 (0.012)	0.94 (0.68–1.31)	0.13 (0.716)
Marital status	Married	12671 (76.2%)	1 (base)		1 (base)	
	Separated/divorced	99 (0.6%)	0.89 (0.33–2.44)	0.05 (0.827)	0.97 (0.35–2.70)	0.003 (0.954)
	Unmarried	2053 (12.3%)	**0.52 (0.39–0.70)**	**18.90 (<0.001)**	0.90 (0.63–1.28)	0.36 (0.551)
	Widow (er)	1813 (10.9%)	**0.54 (0.40–0.74)**	**15.39 (<0.001)**	0.86 (0.61–1.21)	0.76 (0.385)
Employment status	Employee/shopkeeper	779 (4.7%)	1 (base)		1 (base)	
	Farmer	3210 (19.3%)	0.83 (0.60–1.16)	1.21 (0.272)	1.00 (0.70–1.44)	0.00 (0.99)
	Homemaker	7779 (46.8%)	**0.54 (0.39–0.74)**	**14.80 (<0.001)**	1.80 (0.70–1.68)	0.12 (0.726)
	Unemployed	3554 (21.4%)	**0.46 (0.33–0.66)**	**18.46 (<0.001)**	1.12 (0.74–1.71)	0.29 (0.592)
	Semiskilled Worker	1314 (7.9%)	1.04 (0.72–1.50)	0.04 (0.834)	1.25 (0.85–1.83)	1.29 (0.256)
Income per month (Rs)	<1500	12056 (72.5%)	1 (base)		1 (base)	
	1500–4500	2672 (16.1%)	**1.32 (1.07–1.63)**	**6.84 (0.009)**	0.94 (0.72–1.24)	0.19 (0.662)
	4500–7600	1186 (7.1%)	**2.19 (1.72–2.78)**	**40.33(<0.001)**	1.23 (0.90–1.69)	1.74 (0.187)
	7600–11400	323 (1.9%)	**3.12 (2.14–4.55)**	**34.71 (<0.001)**	1.65 (1.07–2.54)	5.09 (0.024)
	≥11400	399 (2.4%)	1.57 (1.00–2.47)	3.90 (0.048)	0.96 (0.59–1.56)	0.02 (0.878)
Random blood glucose (mg/dl)	<200	15488 (93.1%)	1 (base)		1 (base)	
	≥200	1148 (6.9%)	1.38 (1.05–1.80)	5.35 (0.021)	1.08 (0.81–1.44)	0.28 (0.59)
Body mass index (kg/m^2)	<18.5	2911 (17.5%)	1 (base)		1 (base)	
	18.5–25	8862 (53.3%)	**3.07 (2.14–4.40)**	**36.83 (<0.001)**	**1.87 (1.23–2.84)**	**8.69 (0.003)**
	25–30	3511 (21.1%)	**6.43 (4.45–9.28)**	**98.61 (<0.001)**	**2.57 (1.60–4.12)**	**15.27 (<0.001)**
	>30	1310 (7.9%)	**6.59 (4.40–9.86)**	**83.93 (<0.001)**	**2.33 (1.38–3.96)**	**9.85 (0.002)**
Waist-hip ratio	Normal	5856 (35.2%)	1 (base)		1 (base)	
	Increased	10780 (64.8%)	1.14 (0.97–1.35)	2.50 (0.114)	1.03 (0.86–1.23)	0.09 (0.759)
Body weight (kg)	1st quartile (≤46 kg)	4350 (26.1%)	1 (base)		1 (base)	
	2nd quartile (47–55)	4718 (28.4%)	**2.01 (1.48–2.72)**	**20.12 (<0.001)**	1.33 (0.94–1.87)	2.64 (0.104)
	3rd quartile (56–65 kg)	4057 (24.4%)	**3.61 (2.70–4.81)**	**76.14 (<0.001)**	**1.83 (1.28–2.62)**	**10.86 (0.001)**
	4th quartile (>65 kg)	3492 (21.0%)	**5.82 (4.40–7.70)**	**152.31 (<0.001)**	**2.31 (1.53–3.48)**	**15.91(<0.001)**
Oil used in cooking	Sunflower oil	2589 (15.6%)	1 (base)		1 (base)	
	Palm oil	4405 (26.5%)	**0.60 (0.47–0.77)**	**16.64 (<0.001)**	0.83 (0.64–1.08)	1.98 (0.159)
	Groundnut oil	9606 (57.7%)	0.84 (0.69–1.03)	2.86 (0.091)	0.99 (0.81–1.23)	0.001 (0.970)
Smoking	No	15246 (91.6%)	1(Base)		1 (base)	
	Yes	1390 (8.4%)	1.37 (1.06–1.75)	5.97 (0.015)	0.89 (0.65–1.22)	0.54 (0.461)
Alcohol consumption	No	15265 (91.8%)	1 (base)		1 (base)	
	Yes	1371 (8.2%)	**1.64 (1.30–2.08)**	**16.95 (<0.001)**	1.19 (0.88–1.61)	1.23 (0.268)
Family history of hypertension	No	15346 (92.2%)			1 (base)	
	Yes	1290 (7.8%)	**1.44 (1.12–1.85)**	**7.96 (0.005)**	0.98 (0.72–1.32)	0.024 (0.876)
Family history of diabetes	No	15496 (93.1%)			1 (base)	
	Yes	1140 (6.9%)	**1.52 (1.17–1.98)**	**9.86 (0.002)**	1.08 (0.79–1.48)	0.28 (0.634)

Bold values are statistically significant outcomes with P value <0.05.

(95% CI 1.23–2.84) among individuals with BMI between 18.5 kg/m^2 and 25 kg/m^2, 2.57 (95% CI 1.60–4.12) among individuals with BMI between 25 kg/m^2 and 30 kg/m^2, and 2.33 (95% CI: 1.38–3.96) among individuals with BMI greater than 30 kg/m^2 as compared to BMI less than 18.5 kg/m^2. Odds of IDH were 1.83 (95% CI: 1.28–2.62) among individuals weighing in the third quartile (56–65 kg) and 2.31 (1,53–3.48) among individuals weighing in fourth quartile (>65 kg). Overall effect of multivariate logistic regression model was computed as Nagelkerke pseudo R-square, which was 6.9% and model as whole was also significant (Chi-squared test: 330.4, p-value<0.001).

4. Discussion

Significant association of IDH with age, especially between fourth and fifth decade of life, and increased body mass index is similar to the risk factors found in other studies elsewhere.[8–11] Role of IDH as a risk factor of cardiovascular disease has not been studied in depth. However, among middle-aged population, IDH has been reported to be associated with a lower risk of incident acute myocardial infarction,[12] and also, IDH and normotensives have been shown to have nonsignificantly different prognosis for cardiovascular mortality.[13,14] Severity of hypertensive complications were more closely related to mean ambulatory SBP as compared with mean DBP.[15] Contrary to these findings, other studies including the Framingham Heart study found average DBP to be strong predictor of cardiovascular disease among younger men.[5,16–18] Also, the presence of IDH in community dwelling older adults has been shown to be associated with a significantly higher risk of incidence of heart failure and also with a trend towards increased risk of cardiovascular death.[19] It has been reported that younger patients tend to have higher urinary albumin: creatinine ratio with increasing 24-hour diastolic blood pressure and IDH is a determinant of target organ damage in Asia in younger patients.[20] There may be a genetic basis for IDH. Studies have suggested that an association exists between the presence of angiotensin-converting

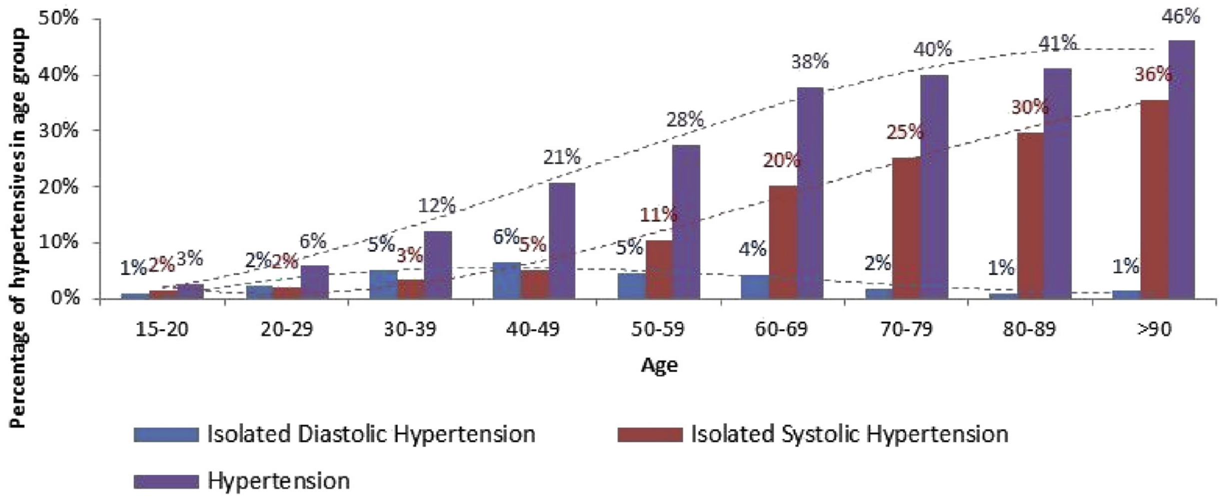

Fig. 1. Plot of prevalence of isolated diastolic hypertension (IDH), isolated systolic hypertension (ISH), and overall hypertension (as per JNC-Classification) in various age groups. A trendline has been added with a polynomial fitting curve of the 3rd order.

enzyme (ACE) genotype deletion (DD) and IDH.[21] It will, therefore, be of immense interest to undertake future research to explore the role of ACE genotype alterations in Indian patients with IDH. While various other mechanisms of IDH have been proposed in literature, the clinical dilemma of choice of treatment with long-term benefits continues to exist.[22,23] Lowering of DBP was found to be associated with reduction of mortality and fatal/nonfatal stroke,[24] but treatment options solely aimed to control IDH have received little or no attention at all in clinical trials. All the guidelines recommend treatment on the basis of both SBP and DBP, not DBP alone. Hence, there are no preferential choices to control IDH other than basing the therapy on factors such as gender, race, and comorbidities. It is, therefore, difficult to choose a “preferred” antihypertensive drug on the basis of DBP. This is especially significant for countries such as India, where the DBP of the general population begins to decline in the fifth decade indicating early changes in arterial walls,[2] making IDH even more relevant. With DBP falling with age, IDH may be altogether missed until the patients are identified with ISH in later age, thereby losing a window of opportunity for timely treatment and reduction of associated cardiovascular mortality and morbidity.

5. Conclusion

There is a significant prevalence of IDH in the semiurban population younger than 50 years of South India. As IDH in young and middle age is known to be associated with increased risk of cardiovascular events and end organ involvement, it highlights the need for study and development of effective management strategies for IDH to reduce associated morbidity and mortality.

Conflicts of interest

All authors have none to declare.

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