Original Article

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

Chetan Mittal a, *, Mandeep Singh b, Tanvir Bakhshi b, S. Ram Babu b, S. Rajagopal b, C. Venkata S. Ram c

a Leisha Hospital, Jalandhar, India
b Total Health Foundation, Chittoor, Andhra Pradesh, India
c Apollo Hospitals, Hyderabad, Telengana, India

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 semi-urban 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 Thavannampalle 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 (±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 semi-urban 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.

© 2019 Cardiological Society of India. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

ARTICLE INFO

Article history:
Received 26 May 2018
Accepted 30 July 2019
Available online 7 August 2019

Keywords:
Isolated diastolic hypertension
Prevalence
Risk factors
Semi-urban
South India
Multivariate logistic regression
Univariate logistic regression
Cardiovascular
Myocardial infarction
WHO STEPS
BMI
Age
Body weight
Odds ratio
Wald Chi-squared value
Blood pressure
Family history
Coronary artery disease
Arterial stiffness

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 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).3 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.4 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).5 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.

* Corresponding author.
E-mail address: cmittal@gmail.com (C. Mittal).

https://doi.org/10.1016/j.ijhj.2019.07.007
0019-4832/© 2019 Cardiological Society of India. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
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:

\[ Z^2 \times \frac{p(1-p)}{C^2} \]

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 \( \pm 1\% \)).

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 \( \pm 1\% \).

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 186 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 (AccuCheckPerforma). 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.9 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 \( \pm 13.6 \)) ISH had a prevalence of 9.7% with a mean age of 60.8 (SD \( \pm 15.3 \)) and with almost equal distribution among the two sexes (male 10.5% and females 9.2%). Mean DBP (\( \pm SD \)) and SBP (\( \pm SD \)) of the surveyed population was 76.5 (\( \pm 12.1 \)) mm of Hg and 123.8 (\( \pm 19.5 \)) 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

| 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) |
BMI between 25 kg/m² and 30 kg/m², and 2.33 (95% CI: 1.38–4.12) among individuals with BMI between 25 kg/m² and 30 kg/m², and 2.33 (95% CI: 1.38–3.96) among individuals with BMI greater than 30 kg/m² as compared to BMI less than 18.5 kg/m². 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 multivariable 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.

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.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 enzyme inhibitors and a genetic polymorphism.
enzyme (ACE) genotype deletion (DD) and IDH.\textsuperscript{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.\textsuperscript{22,23} Lowering of DBP was found to be associated with reduction of mortality and fatal/nonfatal stroke,\textsuperscript{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,\textsuperscript{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.

References

1. Lawes CMM, Vander Hoorn S, Rodgers A. Global burden of blood-pressure-related disease. 2001. Lancet. 2008;371(9623):1513–1518. https://doi.org/10.1016/S0140-6736(08)60655-8.
2. Singh M, Kotwal A, Mittal C, Babu SR, Bharti S, Ram CVS. Prevalence and correlates of hypertension in a semi-rural population of Southern India. J Hum Hypertens. 2017;32(1):66–74. https://doi.org/10.1038/jshh.2017.107.
3. 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. J Am Med Assoc. 2003;289(19):2560–2572. https://doi.org/10.1001/jama.289.19.2560.
4. Kaplan NM, Victor RG, Flynn JT. Kaplan’s Clinical Hypertension. 11th ed. Philadelphia: Wolters Kluwer; 2015.
5. Franklin SS, Larson MG, Khan SA, et al. Does the relation of blood pressure to coronary heart disease risk change with aging? The Framingham Heart Study. Circulation. 2001;103(9):1245–1249.
6. Joshi P, Islam S, Pais P, et al. Risk factors for early myocardial infarction in South Asians compared with individuals in other countries. J Am Med Assoc. 2007;297(3):286–294. https://doi.org/10.1001/jama.297.3.286.
7. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. J Clin Epidemiol. 1996;49(12):1373–1379.
8. Huang J, Wildman RP, Gu D, Munter P, Su S, He J. Prevalence of isolated systolic and isolated diastolic hypertension subtypes in China. Am J Hypertens. 2004;17(10):955–962. https://doi.org/10.1016/j.amjhypert.2004.06.007.
9. Liu F, Adi D, Xie X, et al. Prevalence of isolated diastolic hypertension and associated risk factors among different ethnicity groups in Xinjiang, China. PLoS One. 2015;10(12). https://doi.org/10.1371/journal.pone.0145325.
10. Midha T, Lalchandani A, Nath B, Kumari R, Pandey U. Prevalence of isolated diastolic hypertension and associated risk factors among adults in Kanpur, India. Indian Heart J. 2012;64(4):374–379. https://doi.org/10.4103/0019-5591.107345.
11. Wang Y, Xing F, Liu R, et al. Isolated diastolic hypertension associated risk factors among Chinese in Anhui Province, China. Int J Environ Res Public Health. 2015;12(4):4395–4405. https://doi.org/10.3390/ijerph12044395.
12. Fang J, Madhavan S, Cohen H, Alderman MH. Isolated diastolic hypertension. A favorable finding among young and middle-aged hypertensive subjects. Hypertension. 1995;26(3):377–382.
13. Strandberg TE, Salomaa VV, Vanhanen HT, Pitkälä K, Miettinen TA. Isolated diastolic hypertension, pulse pressure, and mean arterial pressure as predictors of mortality during a follow-up of up to 32 years. J Hypertens. 2002;20(3):399–404.
14. Hozawa A, Ohkubo T, Nagai K, et al. Prognosis of isolated systolic and isolated diastolic hypertension as assessed by self-measurement of blood pressure at home: the Ohasama study. Arch Intern Med. 2000;160(21):3301–3306.
15. Lin JM, Hsu KL, Chiang FT, Tseng CD, Tseng YZ. Influence of isolated diastolic hypertension identified by ambulatory blood pressure on target organ damage. Int J Cardiol. 1995;48(3):311–316.
16. Sesso HD, Stamper MJ, Rosner B, et al. Systolic and diastolic blood pressure, pulse pressure, and mean arterial pressure as predictors of cardiovascular disease risk in Men. Hypertension. 2000;36(5):801–807.
17. Li Y, Wei F-F, Wang S, Cheng Y-R, Wang J-G. Cardiovascular risks associated with diastolic blood pressure and isolated diastolic hypertension. Curr Hypertens Rep. 2014;16(11):489. https://doi.org/10.1007/s11906-014-0489-x.
18. Nirannen TJ, Rissanen H, Johansson JK, Jula AM. Overall cardiovascular prognosis of isolated systolic hypertension, isolated diastolic hypertension and pulse pressure defined with home measurements: the Finn-home study. J Hypertens. 2014;32(3):518–524. https://doi.org/10.1097/HJH.0000000000000707.
19. Sheriff HM, Tsimploulis A, Valentova M, et al. Isolated diastolic hypertension and incident heart failure in community-dwelling older adults: insights from the Cardiovascular Health Study. Int J Cardiol. 2017;238:140–143. https://doi.org/10.1016/j.ijcard.2017.02.142.
20. Wei F-F, Li Y, Zhang L, et al. Association of target organ damage with 24-hour systolic and diastolic blood pressure levels and hypertension subtypes in...
untreated Chinese. *Hypertension*. 2014;63(2):222–228. https://doi.org/10.1161/HYPERTENSIONAHA.113.01940.

21. Jiménez PM, Conde C, Casanegra A, Romero C, Tabares AH, Orías M. Association of ACE genotype and predominantly diastolic hypertension: a preliminary study. *J Renin-Angiotensin-Aldosterone Syst* JRAAS. 2007;8(1):42–44. https://doi.org/10.3317/jraas.2007.006.

22. Odaira M, Tomiyama H, Yoshida M, Shina K, Yamashina A. Isolated diastolic hypertension: possible underlying mechanisms of its development. *Eur Heart J*. 2013;34(suppl_1). https://doi.org/10.1093/eurheartj/eht308.f2370.

23. Laragh JH. Pathophysiology of diastolic hypertension. *Health Psychol*. 1988;7(Suppl):15–31.

24. MacMahon SW, Cutler JA, Furberg CD, Payne GH. The effects of drug treatment for hypertension on morbidity and mortality from cardiovascular disease: a review of randomized controlled trials. *Prog Cardiovasc Dis*. 1986;29(3):99–118. https://doi.org/10.1016/0033-0620(86)90038-1.