

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Changes in Hypertension Prevalence, Awareness, Treatment and Control Rates over Twenty Years in National Capital Region of India- Results from a repeat cross-sectional study.
AUTHORS	Roy, Ambuj; Praveen, Pradeep A; Amarchand, Ritvik; Ramakrishnan, Lakshmy; Gupta, Ruby; Kondal, Dimple; Singh, Kalpana; Sharma, Meenakshi; Shukla, DK; Tandon, Nikhil; Reddy, KS; Anand, Krishnan; Prabhakaran, Dorairaj

VERSION 1 - REVIEW

REVIEWER	Rajeev Gupta Dr Rajeev Gupta, Chairman Preventive Cardiology, Eternal Heart Care Centre & Research Institute, Jaipur, India
REVIEW RETURNED	28-Jan-2017

GENERAL COMMENTS	<p>General:</p> <ol style="list-style-type: none">1. This is a well written manuscript and has answered an important question regarding changes in hypertension prevalence, awareness, treatment and control over 20 years in India.2. The data interpretation is a bit weak and I would suggest some modifications in data analysis.3. The very fact that the studies were performed 20 years apart misses out many changes in macrolevel social structure of the urban and rural areas of India which are important determinants of hypertension. More analyses are required to adjust for factors such as urbanization, human development index, wealth index and social capital. <p>Specific comments:</p> <ol style="list-style-type: none">4. National Capital Region (NCR) is a vague concept and I would suggest that the authors use Delhi urban and Haryana rural locations through out the article. Authors have performed a 4-way comparison- urban vs rural and men vs women and the location specific identification (Delhi is urban and Haryana is rural) would provide better reading.5. The hypertension classification is based on JNC-5. JNC-7 report continued these levels.6. This is not the first study of this type. Chandigarh study published in J Ind Med Assoc (J Indian Med Assoc. 2002 Sep;100(9):547-52, 554-5, 572) and Jaipur Study published in JAPI 2003 (J Assoc Physicians India. 2003 May;51:470-7) were the first to report secular changes in BP levels.7. The Introduction section should include recent reports of hypertension prevalence and control by WHO Group (Lancet 2017) as well as GBD group (JAMA 2017).8. Methods section should include details of method of measurement of BP in both surveys.
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	<p>9. Diagnostic criteria for obesity are not proper. I would suggest that the standard WHO criteria should be used.</p> <p>10. Were measures for waist size or WHR available? These are important hypertension risk factors in South Asians.</p> <p>11. In the Results section please provide 95% confidence intervals for various hypertension prevalence rates.</p> <p>12. Prevalence rates should also be provided after adjusting for various macrolevel (provided above) and individual level risk factors.</p> <p>13. In Table 1 please add 95% confidence intervals for prevalence ratios.</p> <p>14. The conclusions are at variance with results. The rates of awareness, treatment and control have increased remarkably in rural areas. Increasing hypertension awareness in rural areas should also be discussed.</p> <p>15. Limitations sectional should include absence of data on macrolevel factors that not only influence hypertension prevalence but also hypertension control.</p>
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REVIEWER	Mohan, V Madras Diabetes Research Foundation
REVIEW RETURNED	30-Jan-2017

GENERAL COMMENTS	<ul style="list-style-type: none"> • The paper is extremely well written and reviews the changes in hypertension and prevalence in Delhi. Despite limitations such as use of different BP apparatus, the data looks real. • One suggestion would be to give the base line clinical characteristics of the study subjects in survey 1 & 2 as a separate Table 1 and make the present Table 1 as Table 2. • On Page 8, Results section , 4 lines from bottom the use of the word 'diabetics' is to be avoided as it tends to stigmatise. The prevalence was highest in 'people with diabetes' is the right way to phrase it. • The title talks about changes in the national, capital region of Delhi. However, rural Haryana is also included. Hence the title is misleading. Can 'rural Haryana' also be included in the title?
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REVIEWER	Prabhdeep Kaur National Institute of Epidemiology, Chennai (India)
REVIEW RETURNED	21-Feb-2017

GENERAL COMMENTS	<p>Overall comments This is a very useful paper and adds to the existing knowledge on trends in hypertension in India.</p> <p>Section wise comments Abstract</p> <ul style="list-style-type: none"> • Mention the objectives in last sentence of introduction using appropriate scientific terms. (e.g. to estimate the change in prevalence) • Results: Data regarding 2nd line about risk factors is not presented in the paper. Authors have used these variables only as covariates in analysis. Key results from table 2 should be presented here. <p>Methods</p>
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	<ul style="list-style-type: none"> • Use sub headings for clarity such as study population, sample seize, data collection, Anthropometric measurements and lab measurements, operational definitions etc. • Methods Line 2: Sampling frame and sampling strategy need to be explained. It is not clear how the sample was representative of the region. What is the sampling frame? How can you use simple random sampling (rural) for such big population? • Response rate should be written in the results not methods section • Statistical analysis: Methods used for table 2 need to be explained. Whether any interaction terms were used in the analysis. • Characteristics of the study population and risk factors such as BMI, alcohol etc. in 2 surveys should be presented in a table (add new table). Comparison of the characteristics can be done using chi square. • Findings from Table 2 should be elaborated in results. If any interactions were identified in the analysis, it should be explained. • Table 3: provide denominators (N), mention if the data presented is proportions in the top row. Is the population denominator used for all three variables (awareness, treatment, control)? <p>Discussion</p> <ul style="list-style-type: none"> • Page 14: Authors have discussed a lot about risk factors such as education, alcohol however this is not major finding of the survey. This information is not relevant in context of the findings. This can be cut short. • Recommendations need to be elaborated.
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VERSION 1 – AUTHOR RESPONSE

Reviewer-1

General comments:

This is a well written manuscript and has answered an important question regarding changes in hypertension prevalence, awareness, treatment and control over 20 years in India.

The data interpretation is a bit weak and I would suggest some modifications in data analysis. The very fact that the studies were performed 20 years apart misses out many changes in macrolevel social structure of the urban and rural areas of India which are important determinants of hypertension. More analyses are required to adjust for factors such as urbanization, human development index, wealth index and social capital.

Our response: Many thanks for the insightful comments. We agree with the influence of macro level factors on the burden of hypertension in India. However we have not measured these in either of the surveys and are unable to adjust for the same. This limitation has been added in the manuscript as mentioned below.

Specific comments:

1. National Capital Region (NCR) is a vague concept and I would suggest that the authors use Delhi urban and Haryana rural locations throughout the article. Authors have performed a 4-way comparison- urban vs rural and men vs women and the location specific identification (Delhi is urban and Haryana is rural) would provide better reading.

Our response: NCR is a well-defined term coined by an amendment in the Indian constitution and thus we have chosen to use this as the regions selected are part of this. Terming Ballabgarh as representative for rural Haryana may not seem appropriate.

2. The hypertension classification is based on JNC-5. JNC-7 report continued these levels.

Our response: We agree with the reviewer's comments, however, since JNC-7 was the latest iteration at the time of the study we mention it to suggest that the most recent definitions were used for the

study.

3. This is not the first study of this type. Chandigarh study published in J Ind Med Assoc (J Indian Med Assoc. 2002 Sep;100(9):547-52, 554-5, 572) and Jaipur Study published in JAPI 2003 (J Assoc Physicians India. 2003 May;51:470-7) were the first to report secular changes in BP levels.

Our response: We have mentioned ours to be one of the first studies not the first. We also would like to state that ours was the first to study this in representative sample in urban and rural areas. Both the Jaipur and Chandigarh studies were conducted in urban areas only. The Jaipur study has been cited in the discussion.

4. The Introduction section should include recent reports of hypertension prevalence and control by WHO Group (Lancet 2017) as well as GBD group (JAMA 2017).

Our response: We appreciate your suggestion and have added the recent GBD reference published in JAMA (page number-5, paragraph-2, line-10)

5. Methods section should include details of method of measurement of BP in both surveys.

Our response: The details have been provided in method section (page number-6, paragraph-2, line-4)

6. Diagnostic criteria for obesity are not proper. I would suggest that the standard WHO criteria should be used.

Our response: We have changed the cut-offs of obesity according to the WHO cut-offs as suggested. Consequently there is a change in the figure 2 on prevalence of hypertension in obese and in the manuscript (Page-7, paragraph-3, line-9) as cited below.

"World health Organisation cut offs were used to categorise BMI values (normal- BMI<235 kg/m², overweight- BMI 25- <30 kg/m², obesity-BMI≥30 kg/m²) and abdominal obesity [Waist to Hip Ratio (WHR); (>0.90 for men and >0.85 for women)."

7. Were measures for waist size or WHR available? These are important hypertension risk factors in South Asians.

Our response: WHR are available and has been published in our earlier publication. We have now included the prevalence of abdominal obesity (measured in terms of waist hip ratio) among the hypertensive and non-hypertensive population in the result section (Supplementary table-1) and in the logistic regression in Table 2.

8. In the Results section please provide 95% confidence intervals for various hypertension prevalence rates.

Our response: Due to the large sample sizes, the standard errors, as evident from the table-1 are small and hence confidence intervals are very narrow and need to be expressed with at least three decimal places. Thus we have chosen to provide standard errors instead of confidence intervals.

9. Prevalence rates should also be provided after adjusting for various macro level (provided above) and individual level risk factors.

Our response: We did not study macro and health system information, thus it is not possible to adjust for them. We have included this in the limitation (Page 17, first paragraph, line 3). Indeed the changes we observe can be largely explained by macro level factors.

10. In Table 1 please add 95% confidence intervals for prevalence ratios.

Our response: We agree with your suggestion and the 95% CIs of prevalence ratios have been included in Table 1

11. The conclusions are at variance with results. The rates of awareness, treatment and control have increased remarkably in rural areas. Increasing hypertension awareness in rural areas should also be discussed.

Our response: We agree. Since there was no improvement in the overall rates, we have added "overall" in the sentence in the conclusion in the abstract and the main paper. In discussion we have mentioned improvement in rural rates and also stated that it remains lower than urban rates.

12. Limitations section should include absence of data on macro level factors that not only influence hypertension prevalence but also hypertension control.

Our response: Even though we document the change in prevalence and treatment of hypertension, we did not study other macro and health system information which could have helped us explain the change. This has been added to the text. (page number-17, paragraph-1, line-4)

Reviewer:2

1.The paper is extremely well written and reviews the changes in hypertension and prevalence in Delhi. Despite limitations such as use of different BP apparatus, the data looks real. One suggestion would be to give the base line clinical characteristics of the study subjects in survey 1 & 2 as a separate Table 1 and make the present Table 1 as Table 2.

Our response: Many thanks for the comments. The data on other risk factors used for logistic regression has been added in the results as supplementary table 1. The blood pressure prevalence in each risk factor category is presented in figure 2.

2. On Page 8, Results section , 4 lines from bottom the use of the word 'diabetics' is to be avoided as it tends to stigmatize. The prevalence was highest in 'people with diabetes' is the right way to phrase it.

Our response: This was an inadvertent error and we agree with the reviewer. We have made necessary edits in the manuscript as cited below.(page number-9, paragraph-3, line-4)
"The prevalence was highest among those with diabetes followed by those with impaired fasting blood glucose in both urban and rural areas"

3. The title talks about changes in the national, capital region of Delhi. However, rural Haryana is also included. Hence the title is misleading. Can 'rural Haryana' also be included in the title?

Our response: Rural Haryana in this case Ballabgarh is part of NCR, hence the title. We have explained this in detail earlier in response to the comments of reviewer 1.

Reviewer: 3

General comments

This is a very useful paper and adds to the existing knowledge on trends in hypertension in India.

Our response: We thank you for your encouraging comments.

Section wise comments:

1. Abstract: Mention the objectives in last sentence of introduction using appropriate scientific terms. (e.g. to estimate the change in prevalence)

Our response: We have added “prevalence and management.” in the introduction section (Page number-5, paragraph-2, line-4).

2. Results: Data regarding 2nd line about risk factors is not presented in the paper. Authors have used these variables only as covariates in analysis. Key results from table 2 should be presented here.

Our response: The data on other risk factors used for logistic regression has been added in the result section in supplementary table 1.

3. Methods: Use sub headings for clarity such as study population, sample size, data collection, Anthropometric measurements and lab measurements, operational definitions etc.

Our response: We agree and have modified the method section accordingly (sub headings in page 5& 6)

4. Methods Line 2: Sampling frame and sampling strategy need to be explained. It is not clear how the sample was representative of the region. What is the sampling frame? How can you use simple random sampling (rural) for such big population?

Our response: The rural sample was collected from villages which are part of the Ballabgarh Health and Demographic Surveillance System (HDSS). The same set of villages participated in the two surveys and is located in Ballabgarh block of Faridabad district in the state of Haryana, India. Being an HDSS site, it had population level sampling frame and a simple random sampling was used to select households and all eligible individuals from within HDSS households. This has been published in our earlier paper and cited in the manuscript as ref no.11

5. Response rate should be written in the results not methods section

Our response: We agree and have now included the response rate in the result section (page number-8, paragraph-2, line-4)

6. Statistical analysis: Methods used for table 2 needs to be explained. Whether any interaction terms were used in the analysis?

Our response: We agree with your suggestion and the details of methods used for table 2 has been added in the method section and it reads as below

“Logistic regression models were constructed for urban and rural populations separately defining prevalence of hypertension as outcome variable and time period (Survey2 Vs Survey 1) as exposure variables. We added covariates as categorical variables (age groups, gender, obesity, waist-hip-ratio, diabetes and alcohol use), stepwise to the logistic regression model. Adjusted odds ratios and 95% CIs were reported. We also assessed the interaction between time (Survey 1; Survey 2) and other covariates mentioned above using likelihood ratio test. If the interaction was found to be significant, then stratified analysis was reported.”

Accordingly we found a significant interaction between time and age. Hence age stratified models were now added to table -2

7. Characteristics of the study population and risk factors such as BMI, alcohol etc. in 2 surveys should be presented in a table (add new table). Comparison of the characteristics can be done using chi square.

Our response: The demographic characteristics and risk factor profile (with 95% CI) of the study

population has been added to the result section in Supplementary Table 1.

8. Findings from Table 2 should be elaborated in results. If any interactions were identified in the analysis, it should be explained

Our response: We appreciate your suggestions and modified the result section accordingly (Page number-9, paragraph-3, line-7 and significant interaction between time and age was found and is reported.

9. Table 3: provide denominators (N), mention if the data presented is proportions in the top row. Is the population denominator used for all three variables (awareness, treatment, control)?

Our response: The 'N' is the number of all individuals with hypertension. Putting all the Ns makes the Table representation unwieldy. The standard definition for the awareness, treatment, control have been provided in the methodology (page number-7, paragraph-1, line-1-6).

10. Page 14: Authors have discussed a lot about risk factors such as education, alcohol however this is not major finding of the survey. This information is not relevant in context of the findings. This can be cut short.

Our response: This has been discussed in relation to our findings presented in Figure 2 and also in relation to the logistic regression to explain the change in prevalence of hypertension in the population. Further with the rapid transition we have started observing reversal of social gradient for hypertension particularly when education is used as a surrogate. Alcohol is an important but neglected risk factor for hypertension Thus we would request that this be retained.

11. Recommendations need to be elaborated.

Our response: Our conclusion mentions the need for population and patient level interventions to address the increasing burden of CVD and its risk factors.

VERSION 2 – REVIEW

REVIEWER	Rajeev Gupta Eternal Heart Care Centre & Research Institute Jaipur, India
REVIEW RETURNED	27-Mar-2017

GENERAL COMMENTS	No comments.
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REVIEWER	Prabhdeep Kaur National Institute of Epidemiology, Chennai, India
REVIEW RETURNED	25-Apr-2017

GENERAL COMMENTS	Most of the comments have been addressed.
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