

## Original Article

# Using Multistate Observational Studies to Determine Role of Hypertension and Diabetes as Risk Factors for Dementia

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### ABSTRACT

**Background:** Evidence suggests that modifiable risk factors which can be targeted by prevention are vascular diseases, such as diabetes, midlife hypertension (HTN), midlife obesity, midlife cholesterol, mid- and late-life depression as well as lifestyle factors such as smoking, physical inactivity, and poor diet. **Methods:** A comprehensive search of the National Library of Medicine's PubMed database and Google Scholar was conducted. A combinations of medical subject headings and free text words that included search terms related to the exposure (e.g., prevalence, HTN, raised BP, high BP, diabetes, high blood sugar, DM, India, state), were combined with search terms related to the outcomes (e.g., prevalence, disease burden, estimate, dementia, India). The filters included were English for the language category and humans for the study category. **Results:** The PubMed search initially identified 269 references, and a total of 204 abstracts were screened by inclusion criteria. Full-text assessment of 136 articles on prevalence of dementia resulted in 20 relevant articles from which the different regions of the country were identified. Based on the search conducted according to the regions; 287 abstracts of the prevalence of HTN and 577 on the prevalence of diabetes mellitus were screened. There were 43 full-text articles on the prevalence of HTN and diabetes from the regions where the prevalence of dementia was available. Of these potentially relevant articles were 14 in number. **Conclusion:** Despite the uncertainty in the role, the data analysis, therefore, points to a role in the prevention of HTN and diabetes to prevent dementia.

**KEYWORDS:** *Dementia, diabetes, hypertension, multi-state, observational studies, risk*

## INTRODUCTION

The World health organization defines dementia as a syndrome; usually of a chronic or progressive nature, in which there is deterioration in cognitive function (i.e., the ability to process thought) beyond what might be expected from normal aging. It affects memory, thinking, orientation, comprehension, calculation, learning capacity, language, and judgment. Dementia is one of the major causes of disability and dependency among older people worldwide.<sup>[1]</sup>

Worldwide, 47.5 million people have dementia, with just over half (58%) living in low- and middle-income countries. The estimated proportion of the general population aged 60 and over with dementia at a given time is 5–8 per 100 people.<sup>[1]</sup> In 2010, it is estimated that over 3.7 million people are affected by dementia in India.<sup>[2]</sup> This is expected to double by 2030. India's demographic dividend is shifting to aging population and with this the numbers of persons with dementia will double every 5 years of age. Hence, India will have one of the largest numbers of elders with this problem.

Evidence suggests that modifiable risk factors which can be targeted by prevention are vascular diseases, such as diabetes, midlife hypertension (HTN), mid-life obesity,

midlife cholesterol, mid- and late-life depression as well as lifestyle factors such as smoking, physical inactivity, and poor diet.<sup>[1]</sup>

Midlife HTN is a highly predictive parameter of subsequent cognitive deterioration.<sup>[3]</sup> In the Framingham study, cognitive functioning was negatively correlated with the initial systolic and diastolic blood pressure (SBP and DBP, respectively) values measured 12–14 years before.<sup>[4]</sup> Diabetes mellitus (DM) causing micro and macrovascular complications is a well-known risk factor for stroke which if they accumulate or strike vital brain segments may cause dementia.<sup>[5]</sup> A better understanding of the risk factors and identification of factors which would protect or may reduce the risk for dementia is essential for controlling this "silent epidemic."<sup>[1]</sup>

This article reviews major modifiable risk factor such as HTN and DM for dementia through a combination of observational studies.

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## METHODS

### Search strategy

We comprehensively searched the National Library of Medicine's PubMed database and Google Scholar from February to July 2016. We used combinations of medical subject headings (MESH) and free text words that included search terms related to the exposure (e.g., prevalence, HTN, raised BP, high BP, diabetes, high blood sugar, DM, India, state), which were combined with search terms related to the outcomes (e.g., prevalence, disease burden, estimate, dementia, India). The filters included were English for the language category and humans for the study category. We identified articles eligible for further review by performing an initial screen of identified titles or abstracts, followed by a full-text review.

### Selection criteria

Articles included in the review were cross-sectional or cohort; studies conducted among adult populations ( $\geq 18$  years old) published after year 1995. Articles on the prevalence of dementia were searched first and were segregated region wise. The states or regions with reported dementia prevalence were added in the MESH to search-related exposure (DM and HTN) in that state. Since chronic conditions such as cognitive decline start developing years after the incidence of HTN,<sup>[6]</sup> the studies on risk factors obtained were those published before or during the prevalence data of dementia.<sup>[7-23]</sup> HTN was defined as SBP more than or equal to 140 and or DBP more than or equal to 90 mmHg, and DM was defined as fasting blood sugar  $\geq 126$  mg/dl or postprandial blood sugar  $\geq 200$  mg/dl. Articles were excluded if they were letters, abstracts, conference proceedings, case series, case-control studies, reviews, and meta-analysis; not conducted on humans; not community-based studies, and not pertaining to regions with reported dementia prevalence.

### Study selection

Two independent reviewers (Desraj and Mitasha Singh) screened the titles and abstracts of the initially identified studies to determine whether they would satisfy the selection criteria. Any disagreements about selection were resolved through consensus or consultation with a third author (Manoj Kumar Gandhi). Full-text articles were retrieved for the selected titles. Reference lists of the retrieved articles were

searched for additional publications. The retrieved studies were assessed again by two independent authors (Sunil Kumar Raina and Vishav Chander) to ensure that they satisfied the inclusion criteria.

### Data extraction

A data collection form was designed before the implementation of the search strategy. This form was used by two independent reviewers to extract the relevant information from the selected studies (Des Raj and Mitasha Singh). The data collection form included questions on year of publication, design, geographic origin and setting, and information on the reported exposure and outcomes (e.g., percentage of population with dementia, percentage of hypertensive patients, and percentage of diabetic patients).

### Statistical analysis

Regression analysis was run for each of exposure variable (DM and HTN) in linear regression analysis. Pearson's correlation coefficient was presented for both the factors.

## RESULTS

The PubMed search initially identified 269 references, and a total of 204 abstracts were screened by inclusion criteria. Full-text assessment of 136 articles on the prevalence of dementia resulted in 20 relevant articles, from which the different regions of the country were identified. Based on the search conducted according to the regions, 287 abstracts of the prevalence of HTN and 577 on the prevalence of DM were screened. There were 43 full-text articles on prevalence of HTN and diabetes from the regions where the prevalence of dementia was available. Of these potentially relevant articles were 14 in number.

The prevalence of dementia has been studied using different criteria in different regions of the country. The highest prevalence in the above Table 1 was observed from the Southern State of Tamil Nadu from district Vellore (rural area) reported prevalence of 10.6% and from Chennai (urban) reported a prevalence of 7.5% using 10/66 dementia diagnosis criteria.<sup>[2]</sup> The study (10/66) which reported dementia prevalence also reported prevalence of HTN and diabetes in Tamil Nadu.<sup>[24]</sup> The prevalence of HTN (68.6%) and diabetes (12.1%) was higher in urban area as compared to rural (45.6% and 6.6%, respectively).

**Table 1: List of observational studies included**

State	Uttar Pradesh		Punjab		Himachal Pradesh			Kerala	Tamil Nadu		Maharashtra
	Rural	Urban	Rural	Urban	Rural	Urban	Tribe		Rural	Urban	
Dementia prevalence	2.74	6.2	9.3	8.5	1.4	3.2	1.25	3.77	10.6	7.5	4.05
Year of prevalence	2014	2012	2012	2012	2014	2014	2014	2004	2003-2006	2003-2006	2005-2007
Population	728	900	1248	1790	500	500	481	2466	999	1005	2119
HTN prevalence	53.8	32.2	20.4	32.6	37.4	28.1	10.7	54.5	45.6	68.6	30.5
Population	728	1112	2247	839	2749	4000	401	314	445	687	1093
Year of prevalence	2014	2003	2008-2010	2008-2010	2011	2011-2012	2014	2003	2003-2006	2003-2006	2008-2010
DM prevalence			16.1	8.3	14.2		7.8	3.9	12.4	6.6	12.1
Population			900	2247	839		4000	4000	619	999	1004
Year of prevalence			2012	2008-2010	2008-2010		2011-2012	2011-2012	2000	2003-2006	2003-2006

DM: Diabetes mellitus, HTN: Hypertension

In north, Punjab reported a high prevalence of dementia in district Ludhiana, 8.5% in urban, and 9.3% in rural area using Hindi version of Mini-Mental State Examination (HMSE).<sup>[19]</sup> Another study in same region reported a prevalence of 35.9% and 20.9% of HTN in the rural and urban area, respectively.<sup>[18]</sup> The prevalence of DM was also reported to be higher in urban area as compared to rural area (14.2% and 8.3%, respectively).<sup>[20]</sup>

A higher prevalence of dementia was observed in the north, in the state of Uttar Pradesh in an urban area of Lucknow city; 6.2% using MMSE scale followed by Cambridge Examination for Mental Disorders of the Elderly Revised.<sup>[15]</sup> Another study also reported prevalence of dementia as 2.74% using a series of tests from rural area of Varanasi.<sup>[14]</sup> The prevalence of HTN was reported to be higher in rural area of Varanasi; 53.8%<sup>[14]</sup> as compared to urban area of Lucknow (32.2%).<sup>[16]</sup> The prevalence of diabetes in urban area of Lucknow was reported to be 16.1%.<sup>[15]</sup>

The state of Maharashtra in West in a study from urban region of Pune reported the prevalence of dementia to be 4.05%, and the prevalence of HTN and diabetes in this region as reported by India, AB study was 30.9% and 10.9%, respectively.<sup>[22]</sup>

A study by Mathuranaath *et al.*<sup>[12]</sup> from Kerala in the south reported a prevalence of dementia to be 3.77% in an urban area of Thiruvananthapuram using a cognitive screening battery followed by diagnostic evaluation, whereas another study from the same region reported 54.5%<sup>[13]</sup> prevalence of HTN and 12.4% prevalence of DM.<sup>[11]</sup>

A study from Himachal Pradesh in north reported the prevalence of dementia as 3.2% from urban area, 1.4% from rural area, and 1.25% from tribal area using HMSE scale.<sup>[10]</sup> Other studies from same region reported a higher prevalence of HTN from rural area (37.4%) as compared to urban (28.1%)<sup>[8]</sup> and tribal area (10.7%).<sup>[9]</sup> The prevalence of DM was reported to be 7.8% from urban area and 3.9% from tribal area.<sup>[7]</sup>

The prevalence of diabetes and HTN with dementia from Table 1 was subjected to linear regression analysis. Table 2 depicts the Pearson's correlation coefficient of the relation between the prevalence of exposure and outcome. An imperfect positive association was observed for both HTN ( $r = 0.17$ ,  $P = 0.62$ ) and diabetes ( $r = 0.22$ ,  $P = 0.57$ ) with dementia. The same has been shown in scatter plots of Figures 1 and 2.

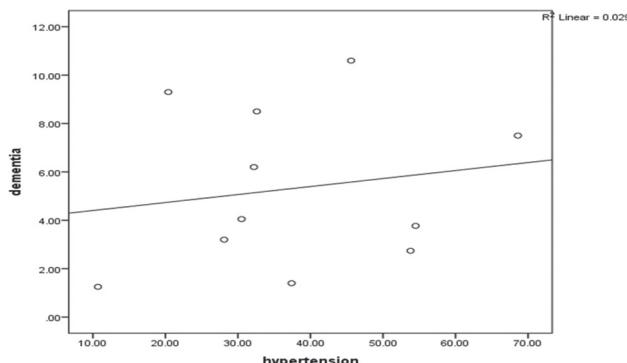


Figure 1: Correlation between prevalence of hypertension and dementia

## DISCUSSION

HTN has been identified as one of the most important controllable risk factors for stroke, which in turn can result in vascular dementia. According to Barnes and Yaffe,<sup>[25]</sup> given the available literature from epidemiological studies and randomized controlled trials only mid-life, not late-life HTN is associated with an increased risk of AD and dementia. About 5% (1.7 million) of AD cases worldwide are potentially attributable to mid-life HTN according to Barnes and Yaffe. According to a review by Biessels *et al.*, of 14 eligible longitudinal population-based studies, the risk of dementia is, in general, increased in patients with DM, and this increased risk seems to include both Alzheimer's disease and vascular dementia.<sup>[26]</sup> On analysis by Pasquier *et al.* of prospective and cross-sectional studies, found evidence of an elevated risk of both vascular dementia and AD in patients with strong interaction of other factors such as HTN, dyslipidemia, and ApoE genotype.<sup>[27]</sup> Pasquier *et al.* also found that DM type 2 to be an independent predictor of poststroke dementia.<sup>[27]</sup> The current study points to a positive association between diabetes, HTN, and Dementia even though the association is not perfect. The results from a study conducted by us previously also pointed to an association between raised BP and dementia although we were not able to establish a relation between diabetes and dementia.<sup>[28]</sup> Although there is uncertainty regarding the relationship between BP and risk of dementia, AlzRisk does promote that the benefits of BP control on cardiovascular risk are sufficient to justify the role of preventing HTN to prevention of dementia. However the same cannot be said of diabetes and dementia.<sup>[29]</sup> According to Biessels *et al.*, there is still a need for studies on large population-based cohorts of elderly people with diabetes.<sup>[26]</sup>

## CONCLUSION

Despite the uncertainty in the role, the data analysis, therefore, points to a role in the prevention of HTN and diabetes to prevent dementia.

Table 2: Regression analysis

Dementia R (correlation coefficient)	P
HTN	0.17
DM	0.22

DM: Diabetes mellitus, HTN: Hypertension

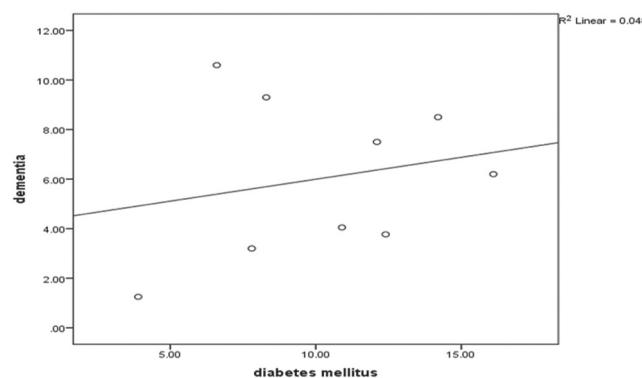


Figure 2: Correlation between the prevalence of diabetes mellitus and dementia

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## Conflicts of interest

There are no conflicts of interest.

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