

Original Research Article

Hypertension and Diabetes as a risk factor for dementia: a cross sectional study

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ABSTRACT

Background: A relation between possible cardiovascular risk factors (hypertension and diabetes) and dementia has been studied in the past and an association has been documented, in spite of some studies pointing to the contrary. Our purpose is to analyze the relation between these risk factors and dementia and add some information to the existing concept and will try to conceptualize the pathogenesis of dementia.

Methods: This was a cross sectional study. Patients were recruited from amongst those presenting to our department by convenient consecutive sampling method after taking consent. Five hundred patients of different types of dementia were enrolled. Hypertension was diagnosed using JNC7 criteria. World health organization (WHO) diagnostic criteria were used to diagnose diabetes mellitus. The open Epi software version 3 was used to find the absolute values after preparing 2×2 table. Continuous quantitative data were analyzed using chi square test. Odds ratio and Risk ratio were also calculated. For all statistical tests, a p Value less than 0.05 was taken to indicate significance.

Results: Study provides the strong positive association of hypertension (HTN) and diabetes mellitus (DM) with vascular dementia (VaD) but the relationship of these risk factors were not positively correlated with other dementia.

Conclusions: Positive association of these risk factors with vascular dementia were found but not with the other types of dementia.

Keywords: Alzheimer disease, Dementia, Diabetes, Hypertension, Vascular dementia

INTRODUCTION

An estimated 47 million people worldwide were living with dementia in 2015 and this number is projected to triple by 2050.^{1,2} In the absence of a disease-modifying treatment or cure, reducing the risk of developing dementia is the major approach to reduce the number of individuals affected. Even when effective treatments become available, risk reduction will likely remain a major strategy in reducing the number of individuals affected; for many non-communicable diseases with

available treatments risk reduction efforts remain a major component of the campaigns against these diseases. The role of diabetes and hypertension as risk factors for dementia has been gaining attention recently but till date still there are no clear cut answer regarding the association of hypertension and diabetes with dementia. That's why we are trying to show the association of these possible risk factors with dementia.

Although hypertension is well known as a cause of vascular dementia (VaD), recent findings highlight the

role of hypertension in the pathogenesis of Alzheimer's disease (AD) as well as mild cognitive impairment (MCI). Mild cognitive impairment (MCI) is regarded as a risk for dementia, and its identification is thought to lead to secondary prevention by controlling the risks for cardiovascular diseases. Recent studies have shown that disruption of diurnal blood pressure (BP) variation was closely associated with cognitive impairment.^{3,4} In several clinical trials, BP lowering with antihypertensive agents was shown to substantially reduce the risk of dementia or cognitive decline. Meta-analyses of clinical trials and prospective, observational, longitudinal, and cross-sectional studies, including a Cochrane review, have not indicated a consistent relationship between high blood pressure and dementia; there is stronger evidence for a link with cognitive decline.⁵⁻⁹ A systematic review of meta-analyses, observational studies, and randomized controlled trials found treatments of hypertension may reduce the risk of cognitive decline.¹⁰

The number of people affected by diabetes mellitus has been growing worldwide. In 2015, the International Diabetes Federation estimated that 415 million people aged 20-79 years had diabetes worldwide, and nearly 75% lived in low-to-middle-income countries (LMIC).¹¹ The number of diabetics will continue to rise with diabetes set to affect 642 million people by 2040, and this will take place especially in regions where economies are transitioning from low-income to middle-income levels.¹¹ Diabetes is a known risk factor for dementia and vascular dementia but the association between diabetes and Alzheimer's disease needs to be better clarified.¹² Several longitudinal studies have shown that diabetes was associated only with VaD, but not with AD.¹³⁻¹⁸ Meanwhile, some studies have shown that DM is associated with increased risk of dementia and AD.¹⁹⁻²⁶

Purpose of the study was to analyze any relation between cardiovascular risk factors (Hypertension and Diabetes) and dementia and on the background of the endpoint will try to discuss probable pathophysiology of different types of studied dementia.

METHODS

Study populations

The study was conducted in the department of Neurology at our tertiary care institute. The patients were recruited from amongst those presenting to our department by convenient consecutive sampling method.

Methodology

The study was duly approved by the Institutional Review Board and Institutional Ethics Committee. Five hundred patients of dementia like AD, Fronto temporal dementia (FTD), VaD, dementia with lewy body (DLB), Parkinson's disease dementia (PDD) were enrolled. Patients of secondary dementia except vascular dementia

were excluded from the study. Those patients were also excluded from the study whose dementia could have been due to reasons like recurrent hypoglycemia, cerebral hypoperfusion and head injury. Patients without reliable caregiver were also excluded from the study. AD was diagnosed using DSM IV TR and National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA) criteria. National Institute of Neurological Disorders and stroke and Association International pour la Neurosciences (NINDS-ARIEN) was used for vascular dementia (VaD). Consensus Neary criteria was used for FTD. Consensus criteria were also used for DLB and PDD for diagnosis. Mini mental examination (MMSE) and Blessed dementia scales were used to assess cognitive function. Hypertension was diagnosed using JNC7 criteria. World health organization (WHO) diagnostic criteria were used to diagnose Diabetes mellitus.

Statistical analysis

The open Epi software version 3 was used to find the absolute values after preparing 2x2 table. Continuous quantitative data were analyzed using chi square test. Risk ratio (RR) and odds ratio (OR) both were calculated because both are comparable in magnitude when the disease is rare but OR can overestimate and magnify risk, especially when the disease is more common like hypertension and should be avoided in such cases if RR can be used. Odds ratio (OR) was calculated with 95% confidence interval. For all statistical tests, a p Value less than 0.05 was taken to indicate significance.

RESULTS

Spectrum of dementia

Alzheimer disease was the most common dementia followed by vascular dementia observed in study population. (Figure1).

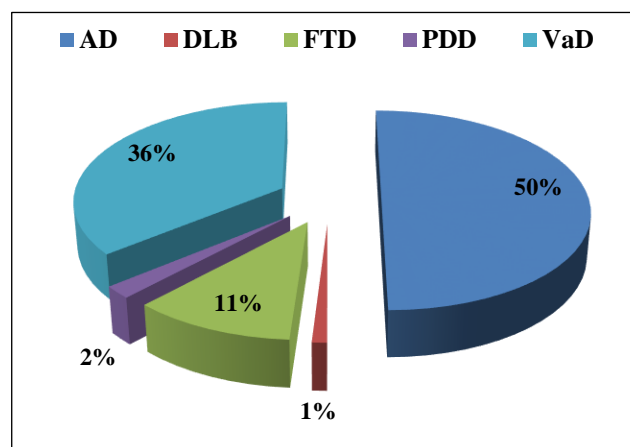


Figure 1: Spectrum of dementia in our study population.

Age of presentation and number of years taken to present after the appearance of symptoms

While analyzing these data interesting observation was noticed that around 80% of the patients of VaD were diagnosed within 3 yrs (Table 1) and the mean age at the time of diagnosis was lesser in VaD in comparison to AD (Table 2).

Relation of hypertension and diabetes mellitus with different dementia

Among different dementia hypertensive and diabetic patients were more common in VaD (Table 3).

Most of the hypertensive patients showed rise in systolic blood pressure only. While analyzing the hypertension as a risk factor for dementia, among all studied dementias, OR were only more than one (>1) in VaD, suggestive of positive correlation, but the confidence interval was >1 also which negated the absolute value of OR.

Table 1: Number of years taken to present after the appearance of symptoms.

		Types of Dementia				
		AD	DLB	FTD	PDD	VaD
Total number of patients		250	5	55	10	180
<3 yrs (n=275)	Number of patients	100	5	20	10	140
	%	40.0%	100.0%	36.36%	100.0%	77.8%
3 - 6 yrs (n=175)	Number of patients	115	0	20	0	40
	%	46.0%	0.0%	36.36%	0.0%	22.2%
>6 yrs (n=50)	Number of patients	35	0	15	0	0
	%	14.0%	0.0%	27.28%	0.0%	0.0%

Table 2: Mean age of the patient.

Types of Dementia	Mean Age(yrs)	Std. Deviation
AD	69.98	8.287
DLB	56	2
FTD	62	5.899
PDD	74	2
VAD	62.38	12.419

Table 3: Association of different Dementia with Hypertension and Diabetes.

		Types of Dementia				
		AD	DLB	FTD	PDD	VaD
Total number of different dementia patients		250	5	55	10	180
HTN (n=146)	Number of patients	45	0	5	1	95
	%	18.0%	0.0%	9.0%	10.0%	52.8%
DM (n=40)	Number of patients	10	0	5	0	25
	%	4.0%	0.0%	9.0%	0.0%	13.8%

Table 4: Relationship of dementia with hypertension (HTN).

Dementia with HTN	Risk ratio	Odds ratio	95% Confidence interval	p value
AD With HTN	0.45	0.3238	0.2150 to 0.4879	<0.0001
VaD with HTN	3.26	5.8950	3.8787 to 8.9596	<0.0001
FTD with HTN	0.28	0.2156	0.0842 to 0.5524	0.0014

Table 5: Relationship of dementia with diabetes mellitus (DM).

Dementia with DM	Risk ratio	Odds ratio	95% Confidence interval	p value
AD with DM	0.333	0.305	0.1460 to 0.6396	0.0017
VaD with DM	3.47	3.279	1.6804 to 6.4007	0.0005
FTD with DM	1.14	1.171	0.4388 to 3.127	0.7521

DISCUSSION

Study started with the holistic approach, with the common pathophysiology of dementia in mind, which is complex and confusing. Diabetes and Hypertension both are cardiovascular risk factors and may cause intracerebral hemorrhage or infarction and white matter changes. Possible common pathologies in the brain that would lead to the development of dementia which were earlier taken into consideration a. Intracerebral infarction or hemorrhage b. white matter changes c. focal brain atrophy d. amyloid deposition.²⁷

Till date still there are lot debates going on regarding the association of hypertension and diabetes with dementia. Few studies were able to show the positive correlation of dementia with these risk factors but some of the studies were inconclusive. None of the earlier studies attempted to show the association of these cardiovascular risk factors with the dementia other than Alzheimer's disease and VaD but in this study all the primary dementia and vascular dementia were included. Inclusion of FTD with VaD and AD to know the vascular mechanism in the pathogenesis of dementia seems slightly out of context but it has been stated earlier that Biswanger syndrome and multi infarct dementia can present as FTD. Most of the studies showed positive correlation of VaD with hypertension and diabetes mellitus, but few studies also indicated a positive correlation of hypertension with Alzheimer's disease.

In this study strong positive correlation of hypertension and diabetes mellitus with vascular dementia were found but the correlation of these risk factors with Alzheimer's disease and FTD were non-significant. Study also showed that VaD presented earlier than AD and the mean age was lesser than AD and the finding also supported the understanding that early life hypertension is more related to dementia than late. This observation in addition to the positive correlation of hypertension and diabetes mellitus with VaD strongly suggested that hypertension and or diabetes in a patient due to atherosclerotic changes in the vessels might leads to silent infarct or hemorrhage and white matter changes in the brain. These pathological changes in the brain might progress into focal atrophy leading to VaD. Results of the study itself suggested that the common cascade hypothesis for the development of all types of dementia is somehow impractical and completely baseless and the study only supported earlier mentioned vascular pathophysiology for vascular dementia.

Now it is quite obvious from the study that pathophysiology of AD and FTD is very different from VaD which strengthen the recent pathophysiological explanation of the development of these dementia. Merit of the study was inclusion of significant number of FTD patients. None of the earlier studies included FTD. Limitation of the study was exclusion of DLB and PDD due to lesser number of patients.

CONCLUSION

This study provides the strong evidence that hypertension and diabetes are a risk factor for VaD but not for other dementia including Alzheimer's disease and FTD. Study results were clearly different from earlier studies having faith on the positive relation of hypertension with the development of Alzheimer's disease. Early and effective treatment of both the risk factors might reduce the chances of vascular dementia.

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