



Association of Cardiovascular and Metabolic Diseases with Risk of Dementia in the Urban Population of North India

Ram B Singh,¹ Agnieszka Wilczynska,² Jan Fedacko,³ Rie Horiuchi,⁴ Toru Takahashi,⁵ Ghizal Fatima,⁶ MA Manal Ismail,⁷ Aminat Magomedova,⁸ Arsha Moshiri,⁹ Mahmood Moshiri⁹

Abstract

Background/Aim: Dementia has become a public health problem due to its association with biological risk factors; obesity, diabetes, hypertension and hypercholesterolaemia. Most of these risk factors, appear to be associated with dementia as well as with risk of coronary artery diseases (CADs) and stroke. This study aimed to find out the association of biological risk factors with cognitive impairment and dementia.

Methods: Cross-sectional survey in a hospital was performed. After written informed consent and approval from hospital ethic committee, all subjects (n = 2002) above 25 years of age (1016 males and 986 females) were randomly selected and recruited from urban population of Moradabad, North India. Clinical data and risk factors were recorded with the help of case record form and validated questionnaires. Assessment of cognitive decline and dementia was made by Singh's memory function rating scale and biological risk factors by physical examination, sphygmomanometer and electrocardiography. The association of biological risk factors with dementia was calculated by multivariate logistic regression analysis after adjustment of age and sex.

Results: Obesity, diabetes, hypertension, CAD and hypercholesterolemia were highly prevalent independent risk factors among patients with dementia. Multivariate logistic regression analysis showed that regardless of age and body mass index, diabetes mellitus and CAD were highly significant (p < 0.001) risk factors of dementia. Hypertension and family history of dementia were weakly but significantly (p < 0.05) associated with dementia.

Conclusion: It is possible that increased frequency of obesity, diabetes, hypertension and CAD may increase the risk of dementia in an ageing population. Prevention and control of these biological risk factors may cause decline in the risk of dementia.

Key words: Western diet; Sedentary behaviour; Mastication; Cardiovascular diseases.

1. Halberg Hospital and Research Institute, Moradabad, India.
2. American Center for Psychiatry and Neurology, Dubai, UAE.
3. PJ Safaric University, Kosice, Slovakia.
4. Mukogawa Women's University, Nishinomiya City, Japan.
5. Graduate School of Human Environmental Medicine, Fukuoka University, Fukuoka, Japan.
6. Era Medical College, Era University, Lucknow, India.
7. School of Natural Sciences, College of Science and Technology, University of Central Lancashire, Preston, England, UK.
8. Lomonosov Moscow State University, Moscow, Russia.
9. International College of Cardiology, Richmond Hill, ON, Canada.

Correspondence:

GHIZAL FATIMA
T: 91 9997794102
E: ghizalfatima8@gmail.com

ARTICLE INFO

Received: 31 January 2023
Revision received: 2 April 2023
Accepted: 2 April 2023

Introduction

According to WHO estimates, the population of people living with dementia, could be as high as 50 million.^{1,2} It seems that by 2030, it may be pro-

jected to increase to 75 million. The frequency of dementia may be estimated to be threefold more by 2050. The global count of dementia in 1990

was 20.2 million, which became 43.8 million in 2016. This increase of 117 % contrasted with a minor increase in age-standardised prevalence of 1.7 %, from 701 cases per 100,000 population in 1990 to 712 cases per 100,000 population in 2016.⁴ It seems that globally, dementia was the fifth leading cause of death, accounting for 2.4 million deaths.⁴ The strength of people with dementia will increase in the Asia-Pacific region, from 23 million in 2015 to almost 71 million by 2050.

It is possible that more than half of the risk of dementia could be due to the modifiable risk factors; obesity, diabetes, smoking and due to ageing.⁴ Diet and lifestyle guidelines proposed by International College of Nutrition and International College of Cardiology emphasise on desirable levels of risk factors and protective factors for prevention of dementia.⁵ Apart from diet and lifestyle factors, age, obesity, diabetes and cardiovascular diseases (CVDs); are major risk factors of dementia.¹⁻⁴ Epidemiological studies indicate that diabetes mellitus,⁶ hypertension,⁷ obesity⁸ and coronary artery disease (CAD)⁹ have been demonstrated to be risk factors that predispose memory dysfunction and dementia. A previous study confirmed that late-life depression is associated with increased risk of dementia and supplied evidence that late-life depression may be an early manifestation of dementia rather than increasing risk for dementia.¹⁰ Later research has found that a longitudinal worsening of CVD risk is associated with midlife cognitive decline and the worsening of single CVD risk factor has been shown to be associated with an increased risk of memory impairment and dementia.¹¹

In previous publications based on subjects of this study, prevalence of behavioural risk factors of dementia was reported¹²⁻¹⁴ and questionnaire for assessment of dementia.¹³ This study, aimed to examine the association of CVDs and diabetes with risk of dementia in an urban population of India.

Methods

Informed consent was achieved from each subject and study was approved by the Institutional Ethic Committee, in accordance with Helsinki Declaration 1964.

This cross-sectional survey included randomly selected 20 streets from the urban area of the city of Moradabad.¹⁵ All the subjects were randomly selected, based on voter's list, with an aim of choosing, 40-100 adults, aged 25 years and above, from each block. The 2222 subjects aged 25 years and above were invited, of which 220 (9.90 %) did not volunteer to participate and rest 2002 (1016 men and 986 women) agreed to be part of this study. Interviews were performed in detail, with the help of pretested and validated questionnaires, for assessment of behavioural risk factors and protective factors, prepared according to the guidelines of WHO and Indian Council of Medical Research. All the subjects were evaluated by a dietitian and physician administered questionnaire, a physical examination and sphygmomanometer, electrocardiogram (ECG) and blood tests.

Criteria for diagnosis of risk factors and dementia

The criteria for the diagnosis of some of the behavioural risk factors; tobacco intake, western type diet, sedentary behaviour and alcoholism as well as memory dysfunction or dementia were based on previous studies and have already been reported in earlier publications.¹²⁻¹⁴ In brief, dementia was diagnosed based on a new questionnaire; Mild memory dysfunction (MMD) was identified if there was possible impairment of memory (score 21-40). Impairment of memory was considered if the score was 41-60. The presence of dementia was identified at score 61-80 on the basis of the instrument.^{12, 13} Low cognitive activity was diagnosed based on questionnaires related with mental work. Sleep disruption was considered in presence of sleep in the night of < 6 hours duration and/or disturbed sleep with frequent awakening. Low education was considered in presence of total education of < 5 years in school.

Criteria for diagnosis of biological risk factors

The diagnosis of biological risk factors of dementia such as hypertension, CAD, obesity, diabetes was based on WHO criteria described earlier.¹⁵ Body mass index (BMI) was calculated and obesity was defined as a BMI > 30 kg/m² and overweight when BMI > 25 kg/m² to 29.9 kg/m². Figures for criteria according to the Indian consensus group for overweight (> 23 kg/m²), were also calculated. Central obesity was considered when waist - hip ratio > 0.90 in males and > 0.80 in females were observed, as suggested in previous studies.

Diabetes mellitus was diagnosed in presence of fasting blood glucose > 7.1 mmol/L (126 mg/dL) and postprandial 2 h after 75 g of oral glucose > 11.2 mmol/L (> 200 mg/dL). Glucose intolerance was diagnosed in presence of fasting glucose between 110-126 mg/dL and postprandial glucose between 180 to 200 mg/dL. The measurement of blood pressure (BP) was made in right arm after 5 minute rest, as reported earlier considering: systolic and diastolic phase V of Korotkoff, after 5 min rest as per guidelines of WHO in all subjects. The diagnosis of high BP was made if systolic BP was 140 mm Hg and above and diastolic BP 90 mm Hg and above.

CAD was identified by: (a) past or present history of myocardial infarction or angina or/and earlier identification of CAD; (b) positive Rose questionnaire and (c) specific findings in the ECG: Minnesota codes 1-1, 4-1, 5-9, 5-2 or 9-2. If all the three criteria were present, then it was diagnosed as CAD. Known CAD was also considered as presence of disease. In addition, affirmative response to Rose questionnaire and ECG with certain specific changes were also considered CAD.¹¹⁻¹³

Biochemical data

Venous blood samples were collected after a fasting of about 10 hours in the morning in all subject for analysis of the blood glucose and blood cholesterol and routine blood tests.

Statistical analysis

The continuous variables were given as mean and standard deviation and prevalence rates in percent. Statistical value of association of various risk factors was found out by multivariate logistic regression analysis. The odds ratios and 95 % confidence intervals were obtained to find out level of significance using multivariate model. This was done after adjustment of age and sex using overall prevalence of cognitive deficit, as the dependent variable. Only p-values < 0.05 and two tailed t-test were considered significant.

Results

The results showed that the prevalence of dementia was significantly greater among subjects above 60 years of age in both sexes and trend was

significant as reported earlier.^{12,13} The prevalence of dementia and/or memory impairment was more common among men compared to women, respectively [84 (8.26 %) vs 53 (5.27 %)] with total prevalence of 6.84 % (n = 137).¹³ The prevalence of biological risk factors such as age above 60 years, diabetes mellitus, CAD were more common among men compared with women (Table 1).

Table 1: Prevalence of biological risk factors and protective factors of dementia among men and women

Risk factors and protective factors of dementia	Men (n = 1016)	Women (n = 986)	Total (n = 2002)
Depression and mood disorders	225 (22.1)	215 (21.8)	440 (22.0)
Protective factors			
Mastication of foods (> 30 mastications/bite)	231 (22.7)	197 (19.9)	428 (21.4)
Biological risk factors			
Age > 60 years	226 (22.2)*	169 (17.1)	395 (19.7)
Diabetes mellitus	81 (8.0)*	52 (5.3)	133 (6.6)
Hypertension	285 (28.0)	248 (25.1)	533 (26.6)
Hypercholesterolaemia	313 (30.8)	317 (32.1)	630 (31.4)
Overweight/obese	321 (31.6)	324 (32.8)	645 (32.2)
Coronary artery disease	132 (13.0)*	98 (9.9)	230 (11.4)

*p < 0.05, **p < 0.01 (Chi square test). Values are number (%); Hypertension: blood pressure > 140/90 mm Hg; Hypercholesterolemia: cholesterol > 5.18 mmol/L; Overweight/obese: body mass index > 25 kg/m²;

The frequency of biological risk factors such as age > 60 years, diabetes mellitus and obesity, were highly prevalent risk factors among patients with dementia whereas hypertension, high cholesterol, CAD and family history of dementia were not very common but frequency was significant. The frequency of risk factors among patients with dementia and those without dementia are given in Figure 1. Depression and mood disorders, diabetes mellitus, hypertension, hypercholesterolaemia, obesity, coronary artery disease and family history of dementia were significantly more common among patients with dementia compared to rest of the subjects. Tobacco and alcohol are not common in women.

Multivariate logistic regression analysis showed that regardless of age and BMI, diabetes mellitus, obesity, age > 60 years and CAD were highly significant (p < 0.001) risk factors of dementia. Hypertension and family history of dementia were weakly but significantly (p < 0.05) associated with dementia. Depression and mood disorders as well as high cholesterol were not associated with dementia (Table 2).

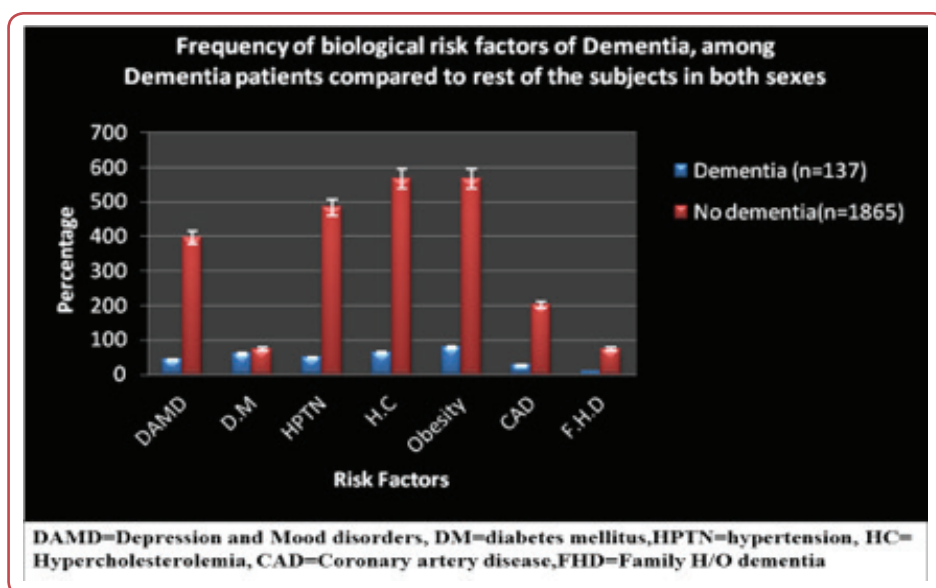


Figure 1: Frequency of biological risk factors of dementia among patients with and without dementia

Table 2: Multivariate logistic regression analysis for association of risk factors with risk of dementia after adjustment of age and body mass index, among men and women

Risk factors	Men (n = 1016)	Women (n = 986)
Depression and mood disorders	0.83 (0.71-0.97)	0.83 (0.71-0.97)
Diabetes mellitus	0.73 (0.66-0.79)**	0.76 (0.70- 0.84)**
Age > 60 years	0.78 (0.70-0.88) **	0.83 (0.75-0.92)**
Hypertension	0.90 (0.81- 0.99) *	0.91 (0.82-0.99)*
Overweight / obese	0.75 (0.68-0.80) **	0.73 (0.66-0.81)**
Coronary artery disease	0.88 (0.81- 0.94) **	0.90 (0.84-0.97)**
Hypercholesterolaemia	0.87 (0.71-0.1.00)	0.91 (0.73-.1.18)
Family history of dementia	0.88 (0.78-0.96) *	0.89 (0.80-0.99)*

* $p < 0.05$, ** $p < 0.001$, p -value was obtained by regression analysis; Values are presented as odds ratios (95 % confidence intervals); Hypertension: blood pressure > 140/90 mm Hg; Hypercholesterolaemia: cholesterol > 5.18 mmol/L; Overweight/obese: body mass index > 25 kg/m²;

Discussion

This study shows that after adjustment of age and BMI, diabetes mellitus, overweight/obesity, age > 60 years and CAD were highly significant ($p < 0.001$) risk factors of dementia. Hypertension, family history of dementia were weakly but significantly ($p < 0.05$) associated with dementia. Depression and mood disorders as well as high cholesterol were not associated with dementia. The overall prevalence of dementia was 6.84 % ($n = 137$) and risk of dementia showed significant increase with increase in age after 55 years as reported earlier.^{12, 13} The population of India

is extremely diverse in terms of socio-economic, lifestyle and behaviour, cultural, linguistic, geographical and genetic factors.¹⁶ The epidemiological transition in India from communicable diseases to non-communicable diseases as well as the unequal disease burden between different states within India is common.¹⁷ These variations in diseases in different states, may be due to varying grades of economic development and alteration in diet and lifestyle factors.¹⁷ Epidemiological studies conducted in India indicate that the prevalence of vascular and metabolic risk factors, as

well as white matter hyper-intensities, differ between urban and rural cohorts.¹⁷⁻²⁰ It seems that the study of the role of vascular risk factors, socioeconomic, cultural factors and genetic influences on dementia prevalence and progression in Indian populations is urgently needed.

In a recent study, involving a total of 62,372 patients, 10,417 (16.7 %) had diabetes and 43,023 (69.0 %) had obstructive CAD.⁹ After a median follow-up of 5.8 years patients with both diabetes and CAD had the highest risk of dementia (aHR 1.47, 95 % CI 1.27-1.71), including Alzheimer's dementia (aHR 1.26, 95 % CI 1.01-1.56) and vascular dementia (aHR 2.60, 95 % CI 1.78-3.80), as well as ischaemic stroke (aHR 2.02, 95 % CI 1.77-2.32). Patients with either diabetes or CAD were at intermediate risk of dementia and ischaemic stroke. No significant trend was observed between the extent of CAD and risk of dementia in diabetes patients (*p* for trend = 0.069). It is possible that both diabetes and CAD were independent risk factors of dementia. Patients with combined diabetes and CAD had a particularly higher risk of cognitive impairment and ischaemic stroke.⁹

There are several studies from India reporting the prevalence and determinants of dementia.²¹⁻²⁶ In an Indian survey among 560 participants, 140 (25 %) patients were identified with impairment of cognition and the risk was higher among rural (27.6 % vs 18.5 %) and female (29.8 % vs 19.1 %) subjects compared to urban subjects, respectively.²¹ The increased risk among rural subjects may be due to lower education and lower quantity of fruits and vegetables in the diet of rural population. In a cohort, comprising of 1066 subjects, 104 had dementia (98 with Alzheimer's dementia - AD) during 8.1 years of follow-up.²² In the elderly subjects, aged ≥ 65 years, the incidence rate was 21.61 per 100,000. These rates of AD, appear to be much greater than that reported from rural north India, comparable with those reported from China and marginally lower than those reported from the Western world.²² The prevalence of biological risk factors of dementia, in a previous study, among 595 elderly subjects > 50 years, was quite high (18.6 %, *n* = 111), because more than 50 % of subjects had either obesity, or hypertension or CAD or diabetes mellitus among urban subjects.²³ A community study was conducted over 5 years (2003-2008) in Kolkata, India, on 100,802 (male: *n* = 53,209) randomly selected subjects to assess prevalence and capture data on incident cases and deaths.²⁴ Standard

case definitions were used. The data were used to estimate years of life lost (YLL) due to premature mortality, years of life lived with disability (YLD) and DALY, based on Global Burden of Disease 2010 approach. In a cohort study among 100,802 subjects, including 53,209 males, there were 103 (55 men) cases of dementia, with a prevalence of 1.53 % (age adjusted 1.12 %) at age ≥ 65 years.²⁴ In those ≥ 55 years age, average annual incidence rate of dementia was 72.57 per 100,000. In a sample of 500 subjects from hill region, mean age 69 years, no subject had dementia which may be due to enormous physical activity, natural environment and traditional diet.²⁵

A rural and urban study included, 750 subjects aged 60 years and above from rural area and 1300 older people 65 years and above from urban area in South India.²⁶ The prevalence of dementia was higher among rural compared to urban subjects (3.5 % vs 2.7 %). It seems that, the only viable option, is to address primary as well as biological risk factors and promotion of protective factors for primary prevention of dementia.^{12, 13, 18} It is possible that the development of an effective systemic health-care model for delivery of services to the families and patients with dementia keeping our sociocultural beliefs in mind may be useful. Every step should be taken to improve awareness regarding dementia and its preventive measures, to halt the epidemic, thereby contributing to the sustainable development goals.^{18, 19} Low-cost, culturally appropriate and modifiable interventions need to be developed expeditiously and implemented through public health measures to reduce the growing burden of dementia.²⁷⁻³⁰ A large cohort study, including 1,958,191 people from UK, with a median age, 55 years and a median follow-up of 9.1 years, showed that dementia occurred in 45,507 people, at a rate of 2.4 cases per 1000 person-years.³⁰ Compared with people of a healthy weight, underweight people (BMI < 20 kg/m² had a 34 % higher (95 % CI 29-38) risk of dementia. Interestingly, the incidence of dementia continued to fall for every increasing BMI category, with very obese people (BMI > 40 kg/m² having a 29 % lower (95 % CI 22-36) dementia risk than people of a healthy weight.

Analysis of demographic data indicate that the patterns of dementia are driven by decline in fertility in conjunction with rise in life expectancy, which together can predispose significant changes in the age structure of the population.³¹ Eco-

conomic development may be associated with many societal changes alongside the rise of non-communicable disease in East Asia, which can alter the prevalence of dementia in the future once those cohorts with high risk of dementia reached their older age.^{32, 33} In a cohort study, involving 6220 subjects (54.8 % females), aged 65 years and older, 463 individuals (7.4 %) had new onset of dementia ascertained in the 12 years of follow up period.³³ In the cohort born between 1926 and 1943, the hazard of developing dementia was 1.68 times greater (hazard ratio [HR] = 1.68 [95 % CI, 1.05-2.86]) for those who were relatively poor compared with those in the highest quintile of wealth, independent of education, index of multiple deprivation and health indicators. The lower risk of dementia among rich people may be due to increased consumption of fruits, vegetables and nuts and better cognitive activity as well as better spare time physical activity. Since diet and lifestyle factors can modulate all the biological risk factors of dementia, hence diet and lifestyle guidelines should be developed along with suitable drug therapy for prevention of dementia.

Conclusion

Biological risk factors such as diabetes mellitus, obesity, CAD, hypertension and stroke should be treated with optimal medical therapy along with modification of behavioural risk factors of dementia. It is possible that improvement in diet and lifestyle factors along with drug therapy of biological risk factors, may be useful in the prevention of dementia.

Acknowledgements

Acknowledgements are given to Sandoz Foundation of Gerontologic Research, Switzerland, for providing funds to conduct this study.

Conflict of interest

None.

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