

Incidence and risk factors of dementia and the primary subtypes in northern rural China

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Abstract

This study was carried out to estimate the incidence and to determine socio-demographic risk factors for dementia among individuals residing in rural northern China.

The current prospective, population-based study was conducted between 2011 and 2016. Follow-up interviews were conducted annually from 2014 to 2016. The study involved 1511 dementia-free individuals aged 60 years or above from rural China. Standard criteria were used to make diagnoses for dementia and Alzheimer disease (AD).

At least one follow up survey was completed with 1181 study participants. At the 5-year follow-up, 127 individuals had developed dementia, 75 had developed AD, and 32 had developed vascular dementia (VaD). With a total of 5649.2 risk years for the sample, the estimated incidence rates per 1000 person-years were 22.48 (95% CI: 18.62, 26.35) for dementia and 13.28 (95% CI: 10.29, 16.26) for AD. Incidence rates for dementia and AD increased with age across the 10-year age groups. Poor education (illiteracy) was an independent risk factor for both AD and VaD. Being engaged in social activities was an independent protective factor for VaD.

The incidence of dementia in rural China was found to be higher than previously reported. Incidence of dementia increased with age, and AD was the most frequent type of dementia. Poor education was associated with a higher risk of VaD and AD. Engagement in social activities was an independent protective factor for VaD.

Abbreviations: AD = Alzheimer disease, CI = confidence interval, ODs = other dementias, VaD = vascular dementia.

Keywords: Alzheimer disease, dementia, incidence

1. Introduction

As the country with the world's largest population, China faces substantial challenges in adjusting to its ageing population, of which an increasing number of individuals will have some degree of dementia. Therefore, investigating the nationwide epidemiology of dementia in rural and urban areas is very important for providing information for developing appropriate policies and patient care strategies. It is especially essential to understand the prevalence and incidence of dementia in rural China, because

70% of the 1.29 billion people in China live in rural areas, and the majority are primarily engaged in agriculture.^[1] A recent meta-analysis estimated that 4.98% to 5.9% of individuals in China aged >60 to 65 years have some type of dementia.^[2,3] Another recent survey regarding the prevalence of dementia in different regions of China found geographic differences in the prevalence of dementia across China, with higher rates of Alzheimer disease (AD) in rural areas compared to urban areas. Moreover, higher prevalence of both vascular dementia (VaD)

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and AD was found in northern China compared to southern China.^[4] Data from our group in 2011 showed that the prevalence rates of dementia, AD, and VaD in individuals aged ≥ 60 years old in rural northern China were 7.7%, 5.4%, and 1.7%, respectively.^[5]

Incidence, the rate of occurrence of a new disease, is a critical measurement for assessing risk and forming causal associations with potential risk factors. Population based longitudinal studies provide the most accurate estimate of the problem as well as the identification of risk and protective factors, but are expensive and time-consuming. Some studies in Western countries have tracked dementia incidence over time. Indeed, statistically significant reductions in the incidence of dementia were reported in 2 U.S. population based studies on African Americans and European Americans.^[6,7] The incidence of dementia over time was also tracked in 1 study done in Bordeaux, France.^[8] Similar annual rates of decline in dementia incidence was also reported in Germany^[9] and the Canadian province of Ontario.^[10] Contrarily, population-based studies conducted in Chicago, IL,^[11,12] and Ibadan, Nigeria^[7] indicated a stable incidence of dementia over 18-year periods.

Most of the current knowledge of dementia epidemiology in China, however, is based on prevalence data. According to prevalence studies, dementia and AD have increased in recent years. Only a few incidences based data were available on dementia in China, which demonstrate an inconsistent trend of incidence of dementia in Chinese individuals. The current study was conducted to estimate the incidence of dementia, AD, and VaD in Chinese individuals residing in rural northern China. We also analyzed the socio-demographic and comorbidities associated with dementia and AD.

2. Method

2.1. Sample

This longitudinal study was carried out in the rural county of Ji in northern China. A full description of the baseline methodology conducted in 2011 has been provided elsewhere.^[5,13,14] The resulting cohort of 1511 dementia-free individuals with complete data was followed up once per year between 2014 and 2016 in 24 villages. Of the 1511 cases, 1181 (78.2%) successfully completed at least one follow-up approximately 3 to 5 years later; 180 (11.9%) had died, while 150 (9.9%) were either untraceable, had travelled or moved, or declined to be interviewed.

The study protocol was approved by the Committee for Medical Research Ethics at Tianjin Huanhu Hospital.

2.2. Screening interview and neurological consultation

Potential subjects were contacted directly by a house visit, at which time they were informed about the objective of the interview and invited to participate. After providing a signed written Informed Consent form, the home interview was conducted by at least two members of a team consisting of 10 medical practitioners. The detailed methods had been described previously.^[5]

2.3. Criteria for dementia and AD

Individuals were classified as having dementia if they fulfilled the criteria listed in the Diagnostic and Statistical Manual of Mental

Disorders, Fourth Edition, Text Revision and had experienced dementia symptoms for ≥ 3 months.^[15,16] Assessments were based on data obtained from the interviews, health examinations, previous records concerning health and social work, and tests for cognitive function and functional capacity. The National Institute of Neurological and Communicative Disorders-AD and Related Disorders Association criteria were used for the clinical diagnosis of AD,^[17] and criteria of the National Institute of Neurological Disorders and Stroke – Association International pour la Recherche en l'Enseignement en Neurosciences were used for the clinical diagnosis of VaD.^[18] Other dementias (ODs), defined by globally accepted criteria included mixed dementia, frontotemporal dementia, dementia with Lewy bodies, Parkinson disease with dementia, alcoholic dementia, hydrocephalus dementia, and post-traumatic dementia.

2.4. Statistical analysis

Incidence rates were calculated by dividing the number of cases with dementia onset in each group by the number of person-years of observation in that group. For subjects with dementia, the number of person-years is calculated by the time from baseline to the halfway point between diagnosis and the previous follow-up examination.

To identify any factors associated with attrition, subjects were divided into 3 mutually exclusive groups:

1. subjects who completed follow-up;
2. subjects who died before follow-up; and
3. subjects who lost during follow-up after the prevalence wave.

Baseline characteristics were compared using one-way analysis of variance models for continuous variables and the chi-square test for categorical variables with Scheffe test, comparing subjects who had completed follow-up with the other 2 groups in a post-hoc analysis.

Subjects were divided into 2 groups: incident dementia and cognitively normal (nondementia). Potential risk factors including baseline characteristics, comorbidities and age at diagnosis were analyzed for the association with incident dementia using the Chi-Squared test. Cox proportional hazard multivariate models were used to identify the effect of demographic variables in the risk of developing dementia, VaD, and AD. P values $< .05$ were considered statistically significant. All data were analyzed using IBM SPSS Statistics for Windows, Version 20.0, Armonk, NY: IBM Corp.

3. Results

Subjects who were deceased before follow-up were significantly older at baseline (73.1 years) than those who either lost during follow-up (68.8 years) or were successfully followed-up (69.3 years), $P < .001$. Individuals who died before follow-up also had a lower education level than those who were lost during follow-up or had a successful followed-up visit (baseline characteristics between the 3 groups presented in Table 1).

The 1181 subjects who were eligible for incidence based assessments included 643 females and 538 males. Of these eligible subjects, 127 developed dementia at the 5-year follow-up. Of the 127 dementia patients, 75 (59.7%) were diagnosed with AD, 32 (24.8%) with VaD, and 20 (15.5%) were diagnosed with ODs including dementia with Lewy bodies, frontotemporal dementia, Parkinson disease dementia, and mixed dementia.

Table 1
Baseline characteristics of follow-up groups.

	N Total = 1511	Deceased N = 180	Lost to follow-up N = 150	Follow-up group N = 1181	P value
Gender					.309
Male	704	91 (50.6)	75 (50.0)	538 (45.6)	
Female	807	89 (49.4)	75 (50.0)	643 (54.4)	
Age (yr) mean (SD)		73.1 (7.6)	68.8 (6.9)	69.3 (6.8)	<.001
Education level					.001
≤5 yr	1196	159 (88.3)	125 (83.3)	912 (77.2)	
>5 yr	315	21 (11.7)	25 (16.7)	269 (22.8)	
Comorbidities					
Hypertension	657	74 (41.1)	70 (46.7)	513 (43.4)	.597
Diabetes mellitus	128	16 (8.9)	8 (5.3)	104 (8.8)	.347
Heart disease	152	16 (8.9)	15 (10.0)	121 (10.2)	.853

With a total of 5649.2 risk years for the sample, the estimated incidence of dementia was 22.48 per 1000 person-years [95% confidence interval (CI): 18.62, 26.35] and that of AD was 13.28 per 1000 person-years (95% CI: 10.29, 16.26), VaD was 5.67 per 1000 person-years (95% CI: 3.71, 7.62). Table 2 Shows the age- and sex-specific average annual incidence rates of dementia, AD, and VaD (new cases per 1000 person-years). The incidence rates of dementia, AD, and VaD increased with age, from 10.24‰ (95% CI: 6.82, 13.67), 4.22‰ (95% CI: 2.01, 6.42), and 4.82‰ (95% CI: 2.46, 7.18) in the young-old (age 60–69 years) to 26.64‰ (95% CI: 19.28, 34.00), 15.77‰ (95% CI: 10.07, 21.46) and 6.53‰ (95% CI: 2.85, 10.20) in those aged 70 to 79 years, to 89.63‰ (95% CI: 64.36, 114.90), 65.19‰ (95% CI: 43.34, 87.03), and 8.15‰ (95% CI: 0.20, 16.10) in the oldest-old (80+ years). This trend of age-specific average annual incidence rates of dementia was similar in men and women.

Participants with incident dementia differed in several respects (baseline age, educational level, history of stroke, alcohol drinkers, widowed/separated and no social activities) from participants without incident dementia (Table 3).

Figure 1 shows the results of the Cox regression analysis for the combined effect of baseline age, educational level, alcohol drinking status, widowed/separated status, social activities, and

history of stroke on dementia onset. When all these terms were included in the regression model, with age used as the time axis, sex was not significantly associated with AD, VaD, or dementia. Illiteracy increased the risk of incidence of VaD (HR = 10.061; 95% CI: 1.299, 77.740) and AD (HR = 3.922; 95% CI: 1.072, 17.632) relative to formal education of more than 5 years. History of stroke increased the risk of VaD (HR = 5.644; 95% CI: 2.791, 11.411), but not AD (HR = 1.581; 95% CI: 0.720, 3.472). Being engaged in social activities decreased the risk of incidence of VaD (HR = 0.375; 95% CI: 0.177, 0.795).

4. Discussion

In this report, we present incidence estimates of dementia for a cohort of an elderly population aged 60 years or above in northern rural China. We obtained an estimate of incidence of 22.48 per 1000 person-years for dementia and 13.28 for AD of the total sample. No significant differences were observed between the sexes. Increasing age was associated with higher risks of the incidence of dementia and AD. Additionally, poor education was associated with a higher risk of vascular dementia and AD. Among the assessed variables at baseline, history of stroke was a risk factor for the incidence of vascular dementia,

Table 2
Incidence of dementia, Alzheimer disease and vascular dementia: person-years at risk, number of cases, and rates by age and sex (95% confidence interval in parentheses).

Age groups, y	Person-years	Dementia		Alzheimer disease		vascular dementia	
		No. of cases	Rate per 1000 person-years	No. of cases	Rate per 1000 person-years	No. of cases	Rate per 1000 person-years
Man							
60–69	1435	12	8.36 (3.65–13.07)	5	3.48 (0.44–6.53)	6	4.18 (0.84–7.52)
70–79	925	21	22.70 (13.10–32.30)	10	10.81 (4.15–17.48)	7	7.57 (1.98–13.15)
80	219.2	19	86.68 (49.43–123.93)	13	59.31 (28.04–90.58)	2	9.12 (0.34–21.71)
All ages	2579.2	52	20.98 (15.33–26.62)	28	11.29 (7.13–15.45)	15	6.05 (3.00–9.10)
Woman							
60–69	1884.2	22	11.68 (6.83–16.53)	9	4.78 (1.66–7.89)	10	5.31 (2.03–8.59)
70–79	914.2	28	30.63 (19.46–41.80)	19	20.78 (11.54–30.03)	5	5.47 (0.69–10.25)
80–	271.6	25	92.05 (57.67–126.43)	19	69.96 (39.62–100.29)	2	7.36 (0.28–17.53)
All ages	3070	75	24.43 (18.97–29.89)	47	15.31 (10.97–19.65)	17	5.54 (2.91–8.16)
Total							
60–69	3319.2	34	10.24 (6.82–13.67)	14	4.22 (2.01–6.42)	16	4.82 (2.46–7.18)
70–79	1839.2	49	26.64 (19.28–34.00)	29	15.77 (10.07–21.46)	12	6.53 (2.85–10.20)
80–	490.8	44	89.63 (64.36–114.90)	32	65.19 (43.34–87.03)	4	8.15 (0.20–16.10)
All ages	5649.2	127	22.48 (18.62–26.35)	75	13.28 (10.29–16.26)	32	5.67 (3.71–7.62)

Table 3
Comparison of baseline demographic and clinical characteristics of participants with incident dementia vs controls.

	Normal cognition (1054) n (%)	Dementia (127) n (%)	P value
Gender			.270
Male	486 (46.1)	52 (40.9)	
Female	568 (53.9)	41 (59.1)	
Age (yr old)			<.001
60–64	371 (35.2)	11 (8.7)	
65–69	287 (27.2)	23 (18.1)	
70–74	202 (19.2)	21 (16.5)	
75–79	131 (12.4)	30 (23.6)	
80–84	50 (4.7)	27 (21.3)	
85–	13 (1.2)	15 (11.8)	
Education (yr)			<.001
Illiterate	371 (35.2)	80 (63.0)	
1–5	426 (40.4)	35 (27.6)	
>5	257 (24.4)	12 (9.5)	
Smoking	264 (25.0)	29 (22.8)	.585
Drinks alcohol	243 (23.1)	20 (15.7)	.062
Widowed/separated	204 (19.4)	48 (37.8)	<.001
No social activities	124 (11.8)	33 (26.0)	<.001
Comorbidities			
Hypertension	450 (42.7)	63 (49.6)	.138
Diabetes mellitus	89 (8.4)	15 (11.8)	.206
Heart disease	109 (10.3)	12 (9.4)	.754
History of stroke	120 (11.4)	32 (25.2)	<.001

but not AD. Furthermore, being engaged in social activities was an independent protective factor for vascular dementia.

Very few prospective follow-up studies examining incidence and determinants of dementia in China have been previously

reported.^[19–22] A systematic review and analysis of epidemiology of AD and other forms of dementia in China from 1990 to 2010 showed that the incidence of dementia in people aged 60 years or above was 9.87 cases per 1000 person-years. The incidence of AD was 6.25 cases per 1000 person-years.^[22] A recent study from Anhui showed the incidence of dementia as 14.7 per 1000 person-years in people aged 60 years or above.^[20] In another multicenter study including 4 regions of China, the crude incidence in people ≥ 65 years was shown to be 12.1/1000 person-years for dementia, 8.2/1000 person-years for AD, and 3.1/1000 person-years for VaD.^[21] These studies reflect the notion that the incidence of dementia has increased in recent years. The current study identified that the incidence of dementia in this northern rural older population was 22.48 per 1,000 person-years for dementia, 13.28 for AD, and 5.67 for VaD, higher than previously reported by other studies in China, but comparable to results from previous estimates in other areas.^[6,11,12]

A decline in age-specific incidence of dementia in developed countries is theoretically possible, driven by changes in exposure to suspected developmental, lifestyle, and cardiovascular risk factors for dementia.^[23] There has been a general trend in many high-income countries toward less smoking, falling total cholesterol and blood pressure levels, and increased physical activity, while the trends in cardiovascular health among older people in many low- and middle-income countries are in an adverse direction,^[24] including an increase in stroke^[25] and ischemic heart disease morbidity and mortality,^[26–28] linked to an epidemic of obesity and increasing blood pressure levels.^[29] In the current study, a history of stroke increased the risk of incidence of dementia, particularly VaD. Controlling stroke and cardiovascular risk factors may, indeed, decrease the incidence of dementia.

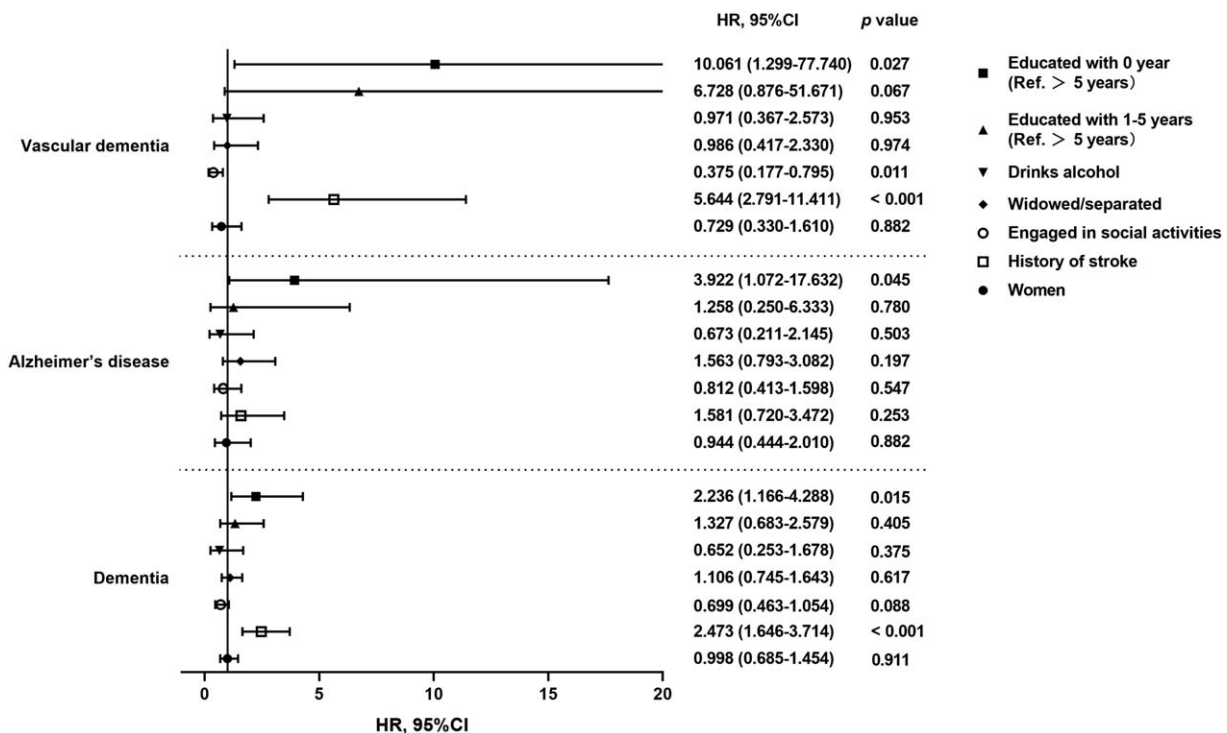


Figure 1. Effect of demographic variables on the risk of dementia and Alzheimer disease and vascular dementia (Cox proportional hazard multivariate models). HR was adjusted for age, sex and education level, drinks alcohol, marriage status, engaged in social activities and history of stroke.

This increase in the incidence of dementia in China can be explained by 3 reasons. Firstly, the relatively smaller sample size, different diagnostic criteria, and different methodologies, and instruments used in Chinese surveys conducted 10 or more years ago may have led to results that show a relatively lower incidence of dementia. Second, the incidence of dementia has, indeed, increased due to the aging population, increased life expectancy, changes in lifestyle, increased risk of stroke, increased levels of obesity, and increased blood pressure levels. As previously suggested, there is evidence that cardiovascular health is deteriorating among older people in China.^[27] The prevalence of smoking among adult men in China is among the highest in the world^[30] and rapid dietary transition is leading to an epidemic of obesity and cardiometabolic disease.^[31] Thirdly, the increased incidence of dementia in this population was mainly as a result of greater dementia in elderly people with a lower reported level of education compared to other studies.

Among the potentially modifiable risk factors, the most consistent evidence involves years of formal education. People with more years of formal education have a lower risk for dementia than those with fewer years of formal education.^[32–37] In the current study, a lack of formal education was an independent risk factor of incidence of vascular dementia and AD. However, varying levels of education had no significant influence in the incidence of dementia. Social activity is highly recognized as an essential component of healthy aging and is associated with a decreased risk of cognitive decline and dementia.^[38–41] In the current study, engagement in social activity was an independent protective factor for VaD. Changing lifestyle habits and keeping active in one's social life may have a positive impact on brain health and dementia risk in later life.

Our study has some limitations. The first is the relatively limited size of the sample with respect to the previous study by Zhang *et al.*, which included 4 centers throughout China, and therefore better represented the genetic heterogeneity of the Chinese population.^[21] However, this data is derived from a population-based, door-to-door survey and the overall response rate was higher than the multicenter survey, with only 9.9% lost to follow up. A second limitation is related to diagnostic validity. In a population survey, contact with participants is more limited than in a clinical setting. In particular in very old adults, it can be difficult to examine and judge the degree of interference within work and social life due to cognitive impairment and comorbidity. We attempted to overcome these difficulties by collecting information from both the subject and a separate informant. Moreover, each diagnosis was made twice, by 2 of 6 board-certificated neurologists from the Dementia Center, and controversial cases were discussed in depth.

5. Conclusion

In general, the current results suggest that the incidence of dementia in rural China may be higher than previously reported. Incidence of dementia increased with age and AD was the most frequent type of dementia. Individuals with less education may have an increased likelihood of developing dementia, with no significant differences observed between males and females. Engagement in social activities was a protective factor for VaD.

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