Prevalence of dementia in rural China: impact of age, gender and education

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Objective – To determine the prevalence of dementia and Alzheimer’s disease (AD) in rural China. Methods – A cross-sectional study was conducted within a cohort of adults older than 50 years of age in Linxian County, China. A Chinese version of the Mini-Mental State Examination (CMMSE) was used to screen cases of possible dementia. Three different cutoff points on CMMSE were applied depending on the participant’s level of education. The participants then were given psychiatric interviews, medical and neurological examinations, and psychometric tests to ascertain the clinical diagnoses of dementia and AD. Results – Among the 16,095 participants, 5.26% were screened positive with 374 diagnosed as having dementia. Among them, AD accounted for 80.5%. The adjusted prevalence rates were 0.33%, 0.89%, 3.43%, and 8.19% in people in age groups 50–54, 55–64, 65–74, and 75 and above, respectively. The prevalence of AD correlated with the participant’s level of education, and was 2.61%, 0.94%, and 0.56% in the illiterate group, in the primary school group, and in the middle school or higher group, respectively. Adjusted by education levels a higher prevalence in women was observed in the illiterate group. Conclusions – The prevalence of dementia in this population is similar to that reported from other areas in mainland China and Taiwan with aging being a significant risk factor. After controlling for age, being a female and having received less number of years of education were associated with an higher prevalence of AD.

There have been several epidemiological surveys of dementia in Chinese populations conducted in Shanghai (1), Beijing (2), and Taiwan (3, 4) where the incidence and prevalence of dementia and Alzheimer’s disease (AD) have been ascertained. Comparing the studies on the prevalence of dementia in Chinese populations age 65 and above, fairly low rates were reported from Taiwan (1.7–3.7%) (5, 6) China (1.8%) (2), and Singapore (1.8–2.5%) (7, 8). In addition, the prevalence of advanced dementia for persons 65 years and older was lower (0.46–1.86%) in China than in western countries (1.3–6.2%) (1). Differences in sampling procedures, data collection methods, and the different diagnostic criteria employed for identifying subjects with dementia are thought to account for most variation in rates reported for China and other countries.

Located in north-central China, Linxian County of Henan Province has been recognized as being nutritionally compromised, and has the highest incidence of esophageal cancer in the world (9, 10). To determine whether dietary supplementation with vitamins and minerals could reduce the incidence and mortality of esophageal and gastric cardia cancer in this area, the National Cancer Institute (NCI), in collaboration with the Cancer Institute of the Chinese Academy of Medical Sciences (CICAMS), Beijing, China, conducted a randomized Nutrition Intervention Trial (NIT)
from 1986 to 1991 (10, 11). Since the completion of the NIT, regular follow-ups have been conducted, with the most recent survey carried out from November 1999 to April 2000. During that survey, neurologists and psychiatrists carried out the current study (the Survey).

In this article, we report the prevalence of dementia and AD in Linxian County and the impact of age, gender, and education. The study was approved by offices of human research protection of each collaborating institution prior to the implementation of the study protocol.

Methods

Study design

Linxian, a rural county of Henan Province, is located on the border of Henan, Hebei and Shanxi provinces. At the time of the Survey, the County had a population of approximately one million, with 11.1% being 55 years and older. This is an agricultural region where wheat farming predominates. The county has no airports. Buses and trains are sole means of long-distance transportation.

The Survey was conducted among the NIT participants residing in four adjacent communes (townships of 1500–2000 dwellings each). Between 1986 and 1991, 29,584 residents, aged 40–69 years, participated in the NIT (9, 10, 12).

Since the completion of the intervention, a series of follow-up evaluations of the trial participants were carried out. During a recent follow-up (November 1999 to April 2000), we invited the cohort members to participate in our Survey. Prior to the Survey, community briefings were given by the study coordinators from CICAMS to explain the consent process, study procedures, and the potential contributions of the study to the understanding of pathogenesis of dementia and AD. Subjects were informed that they could undergo further physical and laboratory evaluations if necessary. Written informed consent was obtained. For those participants who were illiterate or severely demented, the consent was signed by their legal guardian who accompanied them to their visits.

A two-phase procedure was used to assess the prevalence of dementia and AD. In the first phase, a screening of the cohort was conducted to identify participants with cognitive difficulties suggesting dementia. In the second phase, a detailed cognitive and psychiatric evaluation of the participants screened positive was carried out to diagnose dementia and AD.

Eligibility criteria

Participants were deemed eligible if they were in the NIT trial and residing in one of the four participating communes at least 4 days per week or 6 months per year. Among 22,033 eligible cohort members, 16,488 (74.8%) participated in the Survey. There were 5545 eligible residents (25.2%) who did not participate. Of them, 1065 (4.8%) were not able to come to the nearest village health station due to physical limitations. These individuals also declined the offer of taking the shuttle bus provided by the survey team. There were 2367 (10.8%) participants residing away from the County during the entire survey period. The rest of the eligible non-participants included 965 (4.4%) who emigrated out of the NIT participating communes, 171 (0.8%) who were lost to follow-up, and 977 (4.4%) who were otherwise unwilling to participate.

As the Survey was conducted 13 years after the inception of the NIT when the participants were reportedly 40 years of age or older, initially we assumed that all participants would have been at least 53 years old. However, this was not the case for those NIT participants who falsified their ages (for older) to be eligible to receive the nutritional supplements. Such practices were discovered and corrected through subsequent follow-ups. As a result, 12 participants had to be reclassified into younger age groups. However, we did not come across any participants younger than 50 or older than 83 years of age.

The interviews were carried out by the 20 local field testers, who had at least 2 years of post high school education and had participated in the previous NIT follow-up studies. The Survey was conducted in the village health stations located in each commune.

Screening

In the screening phase, there were three sections: collection of demographic information and general medical history, screening with CMMSE, and administration of a brief neurologic examination.

In April and May 1999, as part of a Nutritional Survey during the NIT Followup Study, we joined the NCI-CICAMS study team and examined a subsample (n = 900) of NIT participants. This subsample was randomly selected from three NIT participating communes. The full assessment included (i) a brief medical history, (ii) a physical examination, (iii) a cognitive function assessment, (iv) a neurologic examination, (v) a nutritional questionnaire, and (vi) collection of a blood sample.
for hematologic and biochemical analysis. The objective of this sub-study was to evaluate the then-current nutritional status of participants, to assess the validity of a dietary questionnaire, and to correlate neurologic and cognitive status to vitamin B12 plasma levels that were found lower in Linxian than the average values for Western populations. A separate manuscript is in preparation. For our current study, we piloted a modified version of the CMMSE (mCMMSE) (1, 6). The CMMSE is a culturally adapted version of the MMSE (13) and has been tested in the Chinese population (1) and found to have excellent reliability and validity (1, 13, 14). Most of the items on the CMMSE can be directly applied in Linxian. However, items that require modification include registration, recall, and serial sevens because CMMSE was developed in Shanghai where a distinct southern tone is typified. Linxian is in northern China where the local dialect is markedly different. Thus, to make the pronunciation clearly distinguishable it was necessary to replace ‘rose, ball, and key’ for registration with ‘door, carriage, and pine tree.’ Whereas ‘please close your eyes’ was considered to have a death connotation in Shanghai, and consequently, was replaced with ‘please raise your hands’ (1), people in Linxian did not feel offended by the phrase at all. Thus we kept the original phrase in mCMMSE.

Eight hundred and eighty five of 900 subjects who were tested were able to complete the examination. Among the 15 who were not able to complete the examination, three were hearing impaired, three suffered a recent stroke, and nine had physical disability preventing them from completing the test. The average time of administering the mCMMSE was approximately 10 min. Among the 885 who were able to complete the examination, the mean score was 17.7 (SD: 4.03) on a total score of 30. Seventy five percent of the participants scored ≤21, 50% scored ≤18, and 25% scored ≤15. Without taking into consideration other factors such as age, gender, and level of education, this pilot sample proved to us that mCMMSE was a practical tool for dementia screening in the Linxian population.

Having demonstrated the practicality of mCMMSE in the Linxian population, we needed to determine the cutoff scores based on the levels of education as a marked effect of education on the CMMSE scores was found among Chinese populations (14). In the Shanghai study, cutoff levels of 17, 20, and 24 (of 30) were used for screening subjects with education levels of illiterate (with no formal education), primary school, and middle or high school, respectively. A sensitivity of 85.2% and a specificity of 92.7% for dementia, diagnosed based on DSM-III criteria (15) were reported. We adopted these cutoff points according to the respondent’s level of education (1, 14, 16, 17): 17 for those with no formal education, 20 for those who received 6 years of education or less (primary school), and 24 for participants who had more then 6 years of education (middle or high school).

For participants who could not complete the mCMMSE due to physical impediment such as blindness and deafness, Adult Daily Living (ADL) scale was used to screen them for dementia. ADL greater than 16 was considered screen-positive (18).

Ascertaining the diagnoses

The instruments that were used were administered by psychiatrists who were experienced in psychometric testing under field operating conditions. Testing was carried out in each of the four commune health stations. Some of the examining rooms were transformed into psychiatric testing rooms by having one interview in each room at any given time to minimize potential interruptions. As the walls between the rooms were not very well insulated, we arranged interviews in every other room and leaving the in-between rooms unoccupied to decrease noise transmission.

Based on established age- and education level-dependent cutoff scores on the mCMMSE and/or ADL scales, the subjects who screened positive for dementia were asked to undergo a comprehensive evaluation. The clinical diagnosis of dementia was based on DSM-IV criteria (15). In essence, a diagnosis of dementia required memory impairments with additional cognitive deterioration or personality changes that were severe enough to affect work or social functions, and that the impairments did not date back to childhood and were not secondary to delirium or psychiatric disorders such as depression.

The instruments that were used included a memory test (Fuld Object Memory test) (19, 20), a language test of the categorical fluency (Animal Naming Test) (21), a test of attention and concentration [Digit Span subtest of the Wechsler Intelligence Scale-Revised Chinese (WAIS-RC)] (22), and a test of constructional abilities [Block Design Subtest of the Wechsler Intelligence Scale for Children-Revised (WISC-III)] (23). In addition, to satisfy the DSM-IV criteria that the cognitive impairment has to be sufficient to interfere with social or occupational performance the examiners obtained responses to a dementia history questionnaire, the Pfeffer Functional Questionnaire (24). For differential diagnosis, the
participants were also administered a depression inventory [Center for Epidemiological Studies of Depression (CES-D) scale] and the Hachinski Ischemic Index to assess for evidence of vascular dementia (VsD) (25).

The diagnosis of dementia was determined at the team meetings at which time the study psychiatrists (Drs Zhou, Wu, and Qi) reviewed the data collected from each case. The team meetings regularly took place at the field station centrally located to the four commune health stations on the same day that subjects were administered the neuropsychiatric test battery. Such close proximity between data collection and review was intended to minimize memory lapse for the team psychiatrists and interview staff. The interview staffs were present at the meeting to provide explanations and clarifications if the reviewing psychiatrists had questions regarding data entry and score reporting. At these meetings, the three participating psychiatrists (Drs Zhou, Wu, and Qi) reviewed the cognitive test results, clinical examination and pertinent psychiatric and neurologic history to determine whether the subject met DSM-IV criteria for dementia.

For subjects who met criteria for dementia, the subtype of dementia was further determined. The diagnosis of AD was based on the National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer’s Disease and Related Disorders Association criteria (NINCDS–ADRDA criteria) (26). The diagnosis of VsD utilized the Hachinski score (25) and DSM-IV (15). The Hachinski scale probed for abrupt onset, stepwise deterioration, focal neurologic deficits, hypertension, and a history of stroke. Diagnosis of depression was established on the psychiatric interview that included the Chinese version of Hamilton Depression Inventory (HDI-C) (27) and CES-D. For cases where there was insufficient evidence to establish a specific etiology, the diagnosis of ‘dementia not otherwise specified’ was given.

The diagnoses of subtypes of dementia also required agreement among the three psychiatrists. If the diagnosis was not agreed upon, the cases were reviewed and discussed with the neuropsychologist (Dr Como) at the international team meeting held twice at the field station. These two meetings took place within 2 weeks following each of the two fieldwork periods in November 1999 and April 2000. Detailed analyses of the disagreements were sought and final determination of diagnosis was made at the end of these meetings.

Table 2 and Fig. 1 illustrate the number of participants who were able to complete CMMSE or ADL in the screening phase in each sex; and the number of participants who entered the diagnostic ascertainment phase. As shown, of the 1088 participants screened positive on CMMSE, 200 were also found to be positive by ADL. In addition, 127 were invited to participate in the diagnostic phase as negative controls.

Statistical analysis

The prevalence rates were calculated as the number of cases per 100,000 people on the prevalence day, January 1, 1999, for participants who were 50 years of age or older. Two-independent sample t-test was used to compare the mCMMSE scores between two sexes. One-way ANOVA was applied to compare mCMMSE scores between different levels of education.

Results

Using mCMMSE in screening of dementia

From a probability sample of 22,033 subjects targeted for the screening, a total of 16,488 respondents (74.83%) completed the interview.
The education levels of these participants are shown in Table 1. Reasons for not participating or completing the interview in the remaining 5545 (25.17%) targeted subjects were: (i) unwilling to participate [877 subjects (3.98%)]; (ii) being away from home [2467 subjects (11.2%)]; (iii) emigrating from Linxian County [965 subjects (4.38%)]; (iv) being physically disabled and unable to come to the nearest village health station [1065 subjects (4.83%)]; and (v) being lost to follow-up [171 subjects (0.78%)]. In addition, direct testing could not be performed on 393 subjects who were deaf or blinded.

Among the 16,095 subjects, there were 6504 (40.4%) men and 9591 (59.6%) women, with an average age of 63.39 ± 7.60. Eight thousand eight hundred seventy-six of 16,095 (55.1%) completed 1 year or less of education; 5967 (37.1%) completed 1–6 years of education; and 1252 (7.8%) had more than 6 years of education. The mean mCMMSE score in the entire cohort (n = 16,905) was 23.59 ± 3.76. There was a significant difference on the mCMMSE between men (25.04 ± 3.25) and women (22.60 ± 1.87; P = 0.000). In addition, there were significant group differences on total mCMMSE scores based on their educational levels: 21.72 ± 3.46 for those with 1 year or less of education; 25.51 ± 2.69 for those with 1–6 years of education; and 27.63 ± 1.89 for those with seven and more years of education (P = 0.00).

Prevalence of dementia by gender, education, and age

This phase included participants from the following three categories: (i) 847 participants suspected of dementia based on their performance on mCMMSE; (ii) 114 participants suspected of dementia based on their performance on ADLs; and (iii) 127 participants randomly selected from the negatively screened subjects (the so-called ‘above cutoff’ group) (Table 2 and Fig. 1) These subjects underwent diagnostic evaluations using the neuropsychological battery described in the previous section. Table 3 shows participants’ performance on ADL scale and mCMMSE by the number of years of educations received. Among the 374 patients with dementia, 301 met the diagnostic criteria for AD. In addition, 41 patients met the criteria for VsD. Thirty two did not meet the criteria for either AD or VsD, and as a result were listed as having other non-AD, non-VsD dementia.

Prevalence of AD by gender, education, and age

Three hundred and one patients were diagnosed with AD resulting in an overall prevalence of 1.83%. None of the 118 subjects who screened negative on the mCMMSE met criteria for dementia. Prevalence of AD for subjects aged 55 and older was 2.09%. The prevalence of AD increased with age as shown in Fig. 2 and Table 4. The highest prevalence was 3.57% among men and

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Table 1 Average educational levels of men and women among study participants

<table>
<thead>
<tr>
<th>Years of education received</th>
<th>Male (%)</th>
<th>Female (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Illiterate (&lt;1 year)</td>
<td>1977 (29.6)</td>
<td>7153 (72.9)</td>
<td>9130 (55.4)</td>
</tr>
<tr>
<td>Primary school (1–6 years)</td>
<td>3660 (54.8)</td>
<td>2432 (24.8)</td>
<td>6092 (36.9)</td>
</tr>
<tr>
<td>Middle school or higher (&gt;6 years)</td>
<td>1038 (15.6)</td>
<td>228 (2.3)</td>
<td>1266 (7.7)</td>
</tr>
<tr>
<td>Total</td>
<td>6675 (100.0)</td>
<td>9813 (100.0)</td>
<td>16488 (100.0)</td>
</tr>
</tbody>
</table>

Table 2 Number of subjects in the screening phase and of those in the diagnostic phase in reference to their completion and performance on mCMMSE and ADL

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening phase</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of participants</td>
<td>6675</td>
<td>9813</td>
<td>16488</td>
</tr>
<tr>
<td>Completed CMMSE</td>
<td>6504</td>
<td>9591</td>
<td>16095</td>
</tr>
<tr>
<td>Completed ADL</td>
<td>6550</td>
<td>9642</td>
<td>16192</td>
</tr>
<tr>
<td>Diagnostic ascertainment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of participants</td>
<td>343</td>
<td>745</td>
<td>1088</td>
</tr>
<tr>
<td>CMMSE(+)</td>
<td>154</td>
<td>493</td>
<td>647</td>
</tr>
<tr>
<td>CMMSE(+) and ADL(+)</td>
<td>52</td>
<td>148</td>
<td>200</td>
</tr>
<tr>
<td>ADL(+)</td>
<td>57</td>
<td>57</td>
<td>114</td>
</tr>
<tr>
<td>Negative controls</td>
<td>80</td>
<td>47</td>
<td>127</td>
</tr>
</tbody>
</table>

CMMSE, Chinese version of the Mini-Mental State Examination; ADL, Adult Daily Living.

Table 3 Subjects screened positive for dementia based on performance on ADL scales or mCMMSE in reference to their levels of education

<table>
<thead>
<tr>
<th>Education (year)</th>
<th>On ADLs</th>
<th>On mCMMSE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>&lt;1</td>
<td>33</td>
<td>51</td>
</tr>
<tr>
<td>1–6</td>
<td>18</td>
<td>6</td>
</tr>
<tr>
<td>≥7</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>57</td>
<td>57</td>
</tr>
</tbody>
</table>

ADL, Adult Daily Living; CMMSE, modified version of the Chinese Mini-Mental State Examination.

Figure 2. Prevalence estimates across different age groups and sex, expressed in percentage.
14.1% among women \( (P < 0.01) \). The prevalence of AD was higher in women for each age group. The overall prevalence was 2.24% among women and 1.21% among men \( (P = 0.01) \).

The prevalence of AD correlated with the participant’s level of education. As shown in Table 5, in the illiterate group (defined as 1 year of education or less), the prevalence was 2.61%; in the primary school group (defined as between 1 and 6 years of education) it was 0.94%, and in the middle school or higher group (defined as 7 years of education or higher) it was 0.56%. Post hoc comparisons revealed a significant difference between the illiterate group and the primary or middle school groups. No differences in prevalence were found between the primary school group and the middle school group. Adjusted by education levels the higher prevalence in women was observed only in the illiterate group. At the other two education levels, the prevalence of AD in men was higher than that in women.

### Discussion

In a survey of 3779 rural and urban people older than 60, the prevalence of dementia in Shanghai was 4.21% (based on DSM-IIIR criteria for dementia), with the prevalence of AD estimated at 3.15% (28). The prevalence in that population increased with age: 1.7% in the 60–64 age group; 3.92% in the 70–74 age group; and 12.45% of those older than age 80. Our results were in accordance with these rates.

Furthermore, the observed rate of dementia and AD and its association with age and education are consistent with the general findings in the literature (29). As all participants in the present study were evaluated by psychiatrists with no knowledge of their cognitive test scores, the higher rate of dementia found in the group with little or no formal education could not be explained by possible over-sampling of less educated individuals (30), supporting the notion that education may provide protection against dementia. The mechanisms of such protection, however, remain to be elucidated.

We utilized a two-phase survey methodology: the first phase for finding subjects with suspected dementia by means of the mCMMSE, and the second phase for identifying those with clinical dementia and AD through an intensive clinical evaluation, including the compilation of case histories, performance on physical and neurologic examinations, responses in psychiatric interviews, and a battery of psychometric tests. Such approach provided us with desired rigor. The CMMSE has been widely used as a screening tool for dementia in Chinese (1, 14, 31, 32). While it is well accepted that the CMMSE scores are highly dependent on education (14, 16), we were unable to find any rural community survey of dementia where different cutoff points by educational level were actually applied. However, our population was close to the Shanghai dementia survey (1, 14) in terms of the proportions of subjects who had no formal education (48% vs. 76%), had 1–6 years (28% vs. 20%), and had more than 6 years of education (24% vs. 4%). This educational compatibility between urban and rural community provided us the rationale to utilize cutoff points of the Shanghai study to screen our population to minimize educational bias.

Of note, the ADL procedure included in the screening phase of the study was intended to improve the screening procedure. It was found to be problematic for diagnosing dementia. To that end, we examined its sensitivity and specificity in retrospect and found that it is specific to AD diagnosis but with a rather low sensitivity (37.5%) and rather high specificity (97.9%).

We recognized that a potential problem inherent in the two-step screening procedure, as in the
current study, was the possibility of false negatives in the screening phase. To address this issue, we purposefully invited 127 subjects who screened negative in the screening phase to participate in the diagnostic ascertainment phase, and found that none of them were false negatives.

In the present study, the higher rate of dementia in women disappeared among participants who had at least 1 year of education and persisted in the illiterate group after controlling for education. One possible explanation is that women in those rural regions have less chance to get education than men. Nevertheless, our result is consistent with the Shanghai study in that the higher rate in women was persistent irrespective of the number of years of education received. However, there was no further differentiation between the subjects with 1–6 years of education and those with 1 year or less in that study (1). In another study in Taiwan (30) the higher rate of dementia in women disappeared when adjusted by education levels regardless of the years of education subjects received. This discrepancy was attributed to the different cognitive tests used to screen for dementia. As pointed out by the authors of the Taiwan study, for the illiterate individuals how important the conventional cognitive test findings were in screening and diagnosing dementia remains unclear.

Furthermore, VsD constituted the second cause of dementia in our study, and may include cortical and subcortical VsD. Despite the well-known high prevalence of hypertension in this rural region, the prevalence of VsD was not dramatically elevated when compared with the prevalence of AD which still represents the major cause of dementia. Although it would be preliminary to speculate that the prevalent hypertension in this region was not associated with the risk of VsD, we were not able to discern further whether the vascular risk factors were more prominent in attributing to the reported prevalence of AD.

There were patients who fell into the category of ‘dementia not otherwise specified.’ Some of them had prominent parkinsonism and met DSM-IV, NINCDS-ADRDA criteria of AD diagnosis. Some of them had features suggestive of diagnoses of cortical dementia such as diffuse lewy body disease and frontal temporal dementia. As we did not have the ability to secure the stringent diagnostic criteria for these dementia syndromes, we were only able to appreciate some of the non-AD features on their neuropsychologic testing and anticipate a more technically suitable and more detailed protocol for an expansion of the current study in the near future.

The present study was conducted among the surviving participants of a clinical trial of a prior nutritional intervention. Since the completion of the trial, bi-annual whole- or sub-population follow-up surveys have been carried out to assess changes in nutritional status and general medical conditions of the trial participants, providing evidence of current nutritional deficiency in this population (33–35). In comparison with that reported in the US Boston study (29), we noted a lower prevalence of dementia among subjects older than 75 years of age, possibly due to the poor standard of care in Linxian leading to fewer dementia patients surviving at an older age. Further investigation into issues of this nature would require looking into the differences in population survival and dementia mortality, and the impact of socioeconomic status on the prevalence of dementia between the East and the West. Such pioneering work has been elegantly done elsewhere for us to follow (36,37).

References