Prevalence, Cognitive Characteristics and Influence Factors of Amnestic Mild Cognitive Impairment among Community-dwelling Older Adults in Chengdu, China

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Research Article

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Abstract

Background: Dementia is a global public health priority. Mild cognitive impairment (MCI) is a transitional stage between normal aging and dementia. And amnestic MCI (aMCI) is proved to have a higher probability to develop into AD comparing to other type of MCI. Yet a few studies have focused on prevalence of aMCI in China. This study aims to explore the prevalence of amnestic mild cognitive impairment (aMCI), cognitive characteristics of aMCI, and associated risk factors for aMCI.

Methods: A cross-sectional study was conducted in the communities of Chengdu, China. Participants were 368 older adults aged 60 years and over. Participants completed various neuropsychological assessments, including the Mini-Mental State Examination (MMSE), the Clinical Dementia Rating (CDR), Auditory Verbal Learning Test (AVLT), Wechsler's Logical Memory Task (LMT), Boston Naming Test (BNT) and Trail Making Test Part A (TMT-A). Social information was collected by standard questionnaire. Multiple logistic regression analysis was utilized to screen for the risk and protective factors of aMCI.

Results: Data included 309 subjects with normal cognitive function and 59 with aMCI. The prevalence of aMCI was 16.0%.The average age of participants was 69.06±7.30 years, with 56.0% being females. After controlling for age, gender and education, the Spearman partial correlation coefficient between diverse cognitive assessments and aMCI ranged from -0.52 for the long-term delayed recall scores in AVLT to 0.19 for the time-usage scores in TMT-A, and results revealed that all domains except naming scores (after semantic cue of BNT) and error quantity (in TMT-A) showed statistically significant associations with aMCI. And the results of multiple logistic regression analysis indicated that older age (*OR*=1.044, 95%*CI*: 1.002~1.087, *p*=0.042), lower educational level, and diabetes (*OR*=2.450, 95%*CI*: 1.246~4.818, *p*=0.009) were risk factors of aMCI.

Conclusions: Participants with aMCI showed lower cognitive function in memory, language and executive domains, especially in long-term delayed recall. The participants who were older, had less education, or with diabetes had higher risk of suffering from aMCI. These results may help clinical practitioners design and conduct targeted cognitive training and chronic disease management for the elderly, aiming to prevent and delay development of Alzheimer's dementia.

Background

Alzheimer's Disease (AD) is an increasing public health challenge, causing huge disease burdens for families, health-care systems, and societies as a whole. Currently, there is an estimated 40–50 million people living with dementia [1, 2]. With ageing populations worldwide, this number is projected to increase to 131.5 million by 2050 [1]. Although a large amount of money has been put in developing pharmaceutical treatments for AD, no definitive cure current exists. However, there is growing evidence showing interventions, including pharmaceutical and non-pharmaceutical interventions [3, 4], at an earlier stage would be more likely to delay the onset and progress of AD. If the onset of AD dementia were to be

delayed by 5 years, it would result in a 57% reduction in the number of patients with AD, and save 344 billion to 627 billion US dollars[5].

Mild cognitive impairment (MCI) refers to an impairment in cognition that is greater than normally expected, but has not yet significantly impaired daily function. Many studies have revealed that MCIs are associated with increased risk of progression to AD [6–8]. A review using data collected by the National Alzheimer Coordinating Center in the U.S. found that about 15.8% of MCI progressed to AD with a mean follow-up time of 2.46 years[7]. Glynn found that approximately 32% of people diagnosed with MCI progressed to AD, with a median time of 2 years[6]. Vos's study in Netherlands found that annual conversion rate from MCI to AD was 16.7%[8]. In China, the reported annually conversion rate ranged from 6%-22% [9, 10]. The discrepancies in conversion rates may be due to the different study settings and heterogeneous definitions of MCI.

However, not all people with MCI will develop AD dementia, urging scientists to study clinical subtypes of MCI. Depending on whether memory is affected, MCI can be classified into two clinical subtypes: amnestic MCI (aMCI), where the memory domain is primarily involved, and non-amnestic MCI (naMCI), where the memory of the subject is not impaired. This could further be divided into single domain aMCI, multiple-domain aMCI, single domain naMCI, and multiple-domain naMCI- based on the number of cognitive domains that are impaired [11]. Increasing evidence show that people with aMCI have a higher probability to develop into AD comparing to non-amnestic MCI [12]. A community-based longitudinal study in rural Japan found that the rate of conversion of aMCI patients to dementia was 33.3%, which is higher than that among naMCI patients (17.7%) [13]. Glynn's study showed that those with aMCI are nearly twice as likely to progress to AD than those with naMCI [6]. Therefore, intervention on the progression associated aMCI is critical in terms of delaying AD development.

In the United States, Michau's study found an incidence of 12.4% for aMCI using data from the Uniform Data Set (UDS) of the National Alzheimer's Coordinating Center (NACC) [7]. In Australia, Pusswald found that the incidence was 15.4% for aMCI in the memory outpatient clinic [14]. A Swedish study by Overton showed that the prevalence of aMCI was 7.34% among older adults aged 60 years old and above [15]. In addition, researchers made efforts to identify associated factors for aMCI, and age and education were identified as important risk factors [16–18]. The results of other potential associated factors, including hypertension, diabetes, depression, sleep disturbance, physical exercise, smoking, and drinking, were not shown to be consistent [17, 19, 20].

China is experiencing a rapid growth of its elderly population. AD dementia has become a big public health challenge and will become a huge disease burden in the coming decades. As there is currently no definitive cure for AD, we must prioritize the prevention of AD, including delaying its onset and progression. Given that aMCI is closely related to AD, determining the prevalence and associated risk factors of aMCI is essential when developing preventive approaches towards AD. Three studies reported the prevalence of aMCI in China, which were 12.2%, 16.11% and 17.1%[21–23]. The reported associated factors for aMCI were not consistent as reported in other countries. Due to the inconsistent conclusions

and regional differences in previous research, we performed a study among community dwelling older adults aged 60 years old and above in Chengdu, Sichuan Province, where no related studies have been done yet. In our project, we aim to explore the prevalence of aMCI, the cognitive characteristics of aMCI, and the associated risk factors for aMCI within our population of focus.

Methods

Study design and participants

A sample of urban older adults was obtained from a cross-sectional survey. The survey was conducted in Jinjiang District, one of the twelve districts in Chengdu, Sichuan Province in China. Chengdu is an important central city in western China, ranking eighth in Gross Domestic Product (GDP) among all cities in China, generating 1,217.02 billion yuan in 2016. Jinjiang District also belongs to one of the central districts of Chengdu, ranking fifth in GDP (among all districts in China) with 83.46 billion yuan in 2016. In this area, 21.62% of people were aged 60 years and over in 2016. A multi-stage cluster sampling method was applied to ensure that study participants were selected from various socio-economic sectors, which made it more representative of the population. The eleven towns in Jinjiang District were divided into three levels based on income level – low, middle, and high. Six residential areas were selected randomly from each group, with a total of 18 residential areas. Then we randomly selected three to six buildings from each residential area and investigated all older adults meeting the inclusion criteria. The data was collected from October 2016 to March 2017.

The inclusion criteria for participants were as below: 1) Permanent residents (length of residence ≥ 12 months); and 2) 60 years old and over. Participants were excluded if they: 1) Were unable to complete the survey because of severe visual or hearing impairments, serious physical illness or weakness; 2) Had a history of traumatic brain injuries or psychiatric illnesses that affect cognitive function; 3) Might have major depressive disorders, which was defined as the Chinese self-reported version geriatric depression inventory (GDI-SR) score ≥ 3 [24]; and 3) Were demented or had MCI without memory impairment. In total, 617 randomly selected older adults participated this survey. Among the selected, 13 participants had visual or hearing impairments, 20 refused to answer questions, 84 participants had symptoms of depression, 39 participants gave incomplete data, and 93 participants did not meet the diagnosis of aMCI or normal cognitive function. All in all, 368 older adults were included for analysis.

The survey protocol (including the informed consent) was approved by the Medical Ethics Committee of Sichuan University. All the participants signed the informed consent forms. Qualified research assistants with medical backgrounds and community physicians administered this survey. All the research assistants and clinicians were intensively trained by psychiatrists from the Mental Health Center of West China Hospital.

Cognitive Assessment

All participants completed the following neuropsychological assessments: Mini-Mental State Examination (MMSE), the Clinical Dementia Rating (CDR), Auditory Verbal Learning Test (AVLT), Wechsler's Logical Memory Task (LMT), Boston Naming Test (BNT) and Trail Making Test Part A (TMT-A).

The MMSE scale was used to assess global cognitive function [25]. The MMSE consists of multiple questions and covers six cognitive domains: orientation (10 points), immediate memory (3 points), attention and calculation (5 points), recall ability (3 points), language (8 points), and visuospatial ability (1 point). Usually, the visuospatial ability task was classified as one of the language items. The score totals ranged from 0 to 30, with higher scores indicating better cognitive function.

The CDR is a reliable tool for staging dementia severity [26]. It includes six cognitive categories: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. According to clinical scoring rules, CDR 0 = no dementia, CDR 0.5 = indicates questionable dementia, CDR 1 = mild dementia, CDR 2 = moderate dementia and CDR 3 = severe dementia. In our current study, CDR was also used to obtain information on cognitive complaints and activities of daily living. And the psychiatrists from Mental Health Center of West China Hospital were responsible for CDR rating.

AVLT is a well-recognized measure for verbal learning and memoryB[27]. The examiner read a list of 12 unrelated Chinese words aloud three times. Immediately following each presentation and 20 minutes after the last, the participant was required to recall as many words as possible without a time limit and in any order. The immediate recall scores consisted of the number of words recalled in each trial (range 0-12) and the total number of words recalled in the 3 immediate trials (range 0-36). The delayed score consisted of the number of words recalled after the 20-min delay (range 0-12), which we refer to as the long-term delayed recall in our study. In the end, the participants were shown the word list.

LMT primarily tested participants' logical memory [28]. The participants were told a short story orally, which contained 20 underlining keywords. Then the examinee was asked to recall the story (immediate recall). Approximately 20 or 30 minutes later, free recall of the story was again elicited (delayed recall).

BNT was used as a test for language assessment [29]. The theme of 30 images were asked to be named. If a participant named the item correctly, credits were given for self-corrections and it was recorded among 'spontaneous naming scores (SN)'. If a participant gave a wrong response or gave no response within 20 seconds, the examiner provided a standard semantic cue. If a participant gave the correct answer with the cue, credit was given and was recorded under 'naming scores after phonemic cue (CN)'.

TMT-A was used to assess the execution function of participants [30]. It required the participants to link numbers from 1 to 25 as fast as possible while keeping the nib on the page. The amount of time consumed and the number of errors made were recorded, defined as TMT-A(s) and TMT-A error, respectively.

Social Information

Social information was gathered through participants or their appropriate informants. The following data was collected by standard questionnaire: 1) Demographic data such as age, gender, educational level, marital status and income (average monthly income per person in family); 2) History of chronic diseases including hypertension, diabetes, coronary heart disease and cerebrovascular disease; 3) Daily living information (sleep disorders, smoking and drinking alcohol). Specifically, marital status consisted of two categories: “marriage” and “no marriage”. The latter was defined as being divorced, widowed, or unmarried.

Sleep disorders of older adults were assessed by the Chinese version of Pittsburgh Sleep Quality Index scale (PSQI) [31], which is in the reference period of “past one month”. The scale contains 19 items scored on a 3-point Likert scale and can be divided to 7 domains: subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, use of sleep medications and daytime dysfunction. The global PSQI scores ranged from 0 to 21, with higher total scores indicating worse sleep quality. The Chinese version of the PSQI has been confirmed to show good reliability and validity [32].

Diagnostic Criteria

Diagnosis of aMCI was made based on Petersen’s criteria [33-35] : 1) Memory complaint by participants, preferably corroborated by their informants; 2) Objective memory impairment in addition to a z score $\leq$ -1.5 for at least one memory neuropsychological test and a CDR score of 0.5; 3) Preserved general cognitive function according to MMSE scores adjusted by educational level [36] (>17 for illiterate, >20 for primary school and >24 for above the middle school); 4) Intact daily living ability; and 5) Absence of dementia. Ultimately, among 368 older adults in this study, 59 were aMCI participants and 309 were participants with normal cognitive function.

Statistical Analysis

The continuous variable was presented as mean ± standard deviation (SD) and categorical variables were described in terms of frequency (%). The Spearman correlation coefficient and the Spearman partial correlation coefficient controlling age, gender and educational level were used to detect differences in cognitive test results between the aMCI group and normal group (individuals in the aMCI group were assigned a value of 1 and individuals in the normal group were assigned a value of 0). A comparison of continuous data among aMCI participants and those with normal cognitive function was performed using independent-sample t-test analysis. Chi-square tests were applied to examine group differences in dichotomous variables data. For the ordinal categorical variable (educational level), the Cochran-Armitage test for trend was used to verify whether the prevalence of aMCI is higher with the lower educational level. Multiple logistic regression analysis was utilized to screen for the risk and protective

factors of aMCI. The reported *p* values are the results of two-sided tests. *P* values of <0.05 were considered as statistically significant. Statistical analysis was performed using Stata version 15.1.

Results

Prevalence and Cognitive Characteristics

In this study, the prevalence of aMCI was 16.0%. Comparison of cognitive characteristics between participants with aMCI and participants with normal cognitive function summarized in Table 1. The unadjusted Spearman correlation coefficients ranged from − 0.58 for the AVLT-LR to 0.26 for the TMT-A (s). The results revealed that the scores of participants with aMCI on MMSE, AVLT, LMT and spontaneous naming scores (BNT) were lower than those of cognitively normal participants ($p < 0.05$), and the patients with aMCI consumed longer time and made more errors in TMT-A compared to the normal group ($p < 0.05$). When controlling age, gender and educational level, the Spearman partial correlation coefficient ranged from − 0.52 for the AVLT-LR to 0.19 for the TMT-A (s). The participants in aMCI group also performed worse in most cognitive assessments compared to those in the normal group ($p < 0.05$). While there were no significant differences between groups in naming scores after semantic cue of BNT based on unadjusted or adjusted correlational analysis, we also did not see significant differences in TMT-A error after adjusting for age, gender and education. Using a *z* score ≤ -1.5 for each neuropsychological test, there were 29 (49.2%) aMCI participants with only memory impairment, 13 (22.0%) with memory and language (BNT) impairment, 12 (20.3%) with memory and executive function (TMT-A) impairments, and 5 (8.5%) with memory, language (BNT) and executive function (TMT-A) impairments among participants with aMCI.

Table 1
Cognitive assessment scores in participants with aMCI and normal group

Cognitive assessments	Total (*n* = 368)	aMCI (*n* = 59)	Normal (*n* = 309)	Spearman *ρ*	*p*	Spearman *ρ**	*p*
MMSE	26.56 ± 2.47	24.17 ± 2.98	27.02 ± 2.07	-0.36	< 0.001	-0.29	< 0.001
AVLT							
AVLT-1	2.93 ± 1.66	1.85 ± 1.14	3.14 ± 1.66	-0.28	< 0.001	-0.21	< 0.001
AVLT-2	5.12 ± 2.16	3.12 ± 1.49	5.50 ± 2.05	-0.41	< 0.001	-0.33	< 0.001
AVLT-3	6.28 ± 2.67	3.66 ± 1.61	6.78 ± 2.54	-0.44	< 0.001	-0.37	< 0.001
AVLT-sum 1–3	14.33 ± 5.66	8.63 ± 3.20	15.42 ± 5.36	-0.46	< 0.001	-0.37	< 0.001
AVLT-LR	5.06 ± 2.92	1.19 ± 0.92	5.80 ± 2.56	-0.58	< 0.001	-0.52	< 0.001
LMT							
LMT-IR	5.14 ± 3.22	2.97 ± 2.89	5.55 ± 3.11	-0.31	< 0.001	-0.19	< 0.001
LMT-DR	4.52 ± 3.28	2.49 ± 3.09	4.90 ± 3.18	-0.29	< 0.001	-0.19	< 0.001
BNT							
BNT-SN	19.47 ± 4.35	16.02 ± 4.54	20.13 ± 3.99	-0.32	< 0.001	-0.21	< 0.001
BNT-CN	1.60 ± 2.10	1.64 ± 1.64	1.59 ± 2.18	0.03	0.555	-0.05	0.310
TMT-A							
TMT-A (s)	78.46 ± 41.38	107.75 ± 57.35	72.86 ± 35.00	0.26	< 0.001	0.19	< 0.001

Abbreviations: AVLT-LR, long-term delayed recall scores of Auditory Verbal Learning Test; LMT-IR, immediate recall scores of Logical Memory Test; LMT-DR, delayed recall scores of Logical Memory Test; BNT-SN, spontaneous naming scores of Boston Naming Test; BNT-CN, naming scores after semantic cue of Boston Naming Test.

*Spearman partial correlation coefficient for the association between aMCI and normal group (the aMCI group was assigned a value of 1, and the normal group was assigned a value of 0), controlled for age, gender, and educational level.

Cognitive assessments	Total (*n* = 368)	aMCI (*n* = 59)	Normal (*n* = 309)	Spearman *ρ*	*p*	Spearman *ρ**	*p*
TMT-A error	0.92 ± 2.26	1.68 ± 2.82	0.78 ± 2.11	0.19	< 0.001	0.08	0.151

Abbreviations: AVLT-LR, long-term delayed recall scores of Auditory Verbal Learning Test; LMT-IR, immediate recall scores of Logical Memory Test; LMT-DR, delayed recall scores of Logical Memory Test; BNT-SN, spontaneous naming scores of Boston Naming Test; BNT-CN, naming scores after semantic cue of Boston Naming Test.

*Spearman partial correlation coefficient for the association between aMCI and normal group (the aMCI group was assigned a value of 1, and the normal group was assigned a value of 0), controlled for age, gender, and educational level.

Sociodemographic and Clinical Characteristics

In this study, the average age of participants was 69.06 ± 7.30 years old. Female participants accounted for 56.0%, and participants with a middle school education and above accounted for 60.3%. The participants' sociodemographic and clinical characteristics were presented in Table 2. The age, prevalence of hypertension and diabetes between participants with aMCI, and normal group were statistically different ($p < 0.05$). And the results of Cochran-Armitage test for trend indicated that the prevalence of aMCI was increased with decreasing educational level ($p < 0.05$). However, participants with aMCI and participants in the normal group did not differ in gender, marital status, income, coronary heart disease, cerebrovascular disease, sleep disorders, smoking or drinking.

Table 2
Comparison of sociodemographic and clinical characteristics between participants with aMCI and normal group

Variables	Total (*n* = 368)	aMCI (*n* = 59)	Normal (*n* = 309)	t/χ^2	*p*-value
Demographic factors					
Age (Mean ± SD)	69.06 ± 7.30	72.97 ± 9.06	68.32 ± 6.68	-4.60	< 0.001
Gender (%)				0.32	0.572
Male	162 (44.0)	24 (14.8)	138 (85.2)		
Female	206 (56.0)	35 (17.0)	171 (83.0)		
Education (%)				40.96	< 0.001
Above middle school	222 (60.3)	16 (7.2)	206 (92.8)		
Primary school	102 (27.7)	24 (23.5)	78 (76.5)		
Illiteracy	44 (12.0)	19 (43.2)	25 (56.8)		
Marital status (%)				2.46	0.117
Marriage	301 (81.8)	44 (14.6)	257 (85.4)		
No marriage	67 (18.2)	15 (22.4)	52 (77.6)		
Income (%)				0.02	0.882
>3000 yuan	109 (29.6)	17 (15.6)	92 (84.4)		
≤3000 yuan	259 (70.4)	42 (16.2)	217 (83.8)		
Chronic diseases					
Hypertension (%)				8.54	0.003
No	195 (53.0)	21 (10.8)	174 (89.2)		
Yes	173 (47.0)	38 (22.0)	135 (78.0)		
Diabetes (%)				10.43	0.001
No	289 (78.5)	37 (12.8)	252 (87.2)		
Yes	79 (21.5)	22 (27.9)	57 (72.1)		
Coronary heart disease (%)				0.18	0.672
No	330 (89.7)	52 (15.8)	278 (84.2)		

Abbreviations: SD, standard deviation.

Variables	Total (*n* = 368)	aMCI (*n* = 59)	Normal (*n* = 309)	t/χ^2	*p*-value
Yes	38 (10.3)	7 (18.4)	31 (81.6)		
Cerebrovascular disease (%)				2.38	0.123
No	332 (90.2)	50 (15.1)	282 (84.9)		
Yes	36 (9.8)	9 (25.0)	27 (75.0)		
Daily living information					
Sleep disorders (Mean ± SD)	6.07 ± 4.23	6.41 ± 4.45	6.01 ± 4.19	-0.66	0.509
Smoking (%)				2.55	0.110
No	304 (82.6)	53 (17.4)	251 (82.6)		
Yes	64 (17.4)	6 (9.4)	58 (90.6)		
Drinking (%)				1.81	0.178
No	141 (38.3)	18 (12.8)	123 (87.2)		
Yes	227 (61.7)	41 (18.1)	186 (81.9)		
Abbreviations: SD, standard deviation.					

Risk factors

In the multiple logistic regression analysis, our model included sociodemographic and clinical characteristics that were statistically associated with the prevalence of aMCI. As such, age, educational level, hypertension, and diabetes were selected. Considered as a confounder, gender was also placed in the model. The results shown in Table 3 demonstrate that older age (*OR* = 1.044, 95%*CI*: 1.002 ~ 1.087, *p* = 0.042), obtaining less education, and having diabetes (*OR* = 2.450, 95%*CI*: 1.246 ~ 4.818, *p* = 0.009) were risk factors of aMCI. Particularly, the risk of aMCI among the illiterate (*OR* = 8.161, 95%*CI*: 3.402 ~ 19.575, *p* < 0.001) was nearly twice as high compared to those with primary school education (*OR* = 3.746, 95%*CI*: 1.816 ~ 7.724, *p* < 0.001), using participants with middle school education or above as a baseline (95% CI of 1.000). However, no statistical association with the prevalence of aMCI was seen with gender and hypertension (*p* > 0.05).

Table 3
Multiple logistic regression analysis of risk factors for aMCI

Variables	*B*	*SE*	*Wald* score	*p*-value	*OR*	95%*CI*
Age	0.043	0.021	2.040	0.042	1.044	1.002 ~ 1.087
Gender						
Male	—	—	—	—	—	1.000
Female	-0.252	0.330	-0.760	0.445	0.777	0.407 ~ 1.485
Education level						
Above middle school	—	—	—	—	—	1.000
Primary school	1.321	0.369	3.580	< 0.001	3.746	1.816 ~ 7.724
Illiteracy	2.099	0.446	4.700	< 0.001	8.161	3.402 ~ 19.575
Hypertension						
No	—	—	—	—	—	1.000
Yes	0.573	0.324	1.770	0.077	1.773	0.940 ~ 3.343
Diabetes						
No	—	—	—	—	—	1.000
Yes	0.896	0.345	2.600	0.009	2.450	1.246 ~ 4.818

Abbreviations: SE, Standard Error; OR, Odds Ratio; CI, Confidence Interval.

Discussion

To the best of our knowledge, this is the first study in Western China focusing on the prevalence and characteristics of aMCI and its associated factors among older adults in the community aged 60 years and over. We found that the prevalence of aMCI among older adults in community-dwellings in Chengdu was 16.0%, which is similar to the prevalence found by Li (the prevalence of 17.1% for aMCI among the older adults aged 60 years old and above) [21], and Zhang (the prevalence of 16.1% for aMCI among older adults in Shijiazhuang) [23] in China. The reported prevalence rates of aMCI in many other countries were between 7.3%-11.6%, which were lower than that in China, including our study [15, 18, 37, 38]. One explanation is that different survey scales, sample size, and sampling methods might impact the prevalence rates within different cultural contexts. Another potential explanation is that early life experiences can drastically influence cognitive health in later in life. Our participants were born before 1957, meaning they may have experienced the Great Famine in the early 1960s, which led to malnutrition while growing up. To further amplify these trends, they may have experienced the Cultural Revolution,

during which education was discouraged. Education is an important protective factor against cognitive decline.

After adjusting for age, gender and education, we found that almost all global cognitive function and individual neuropsychological domains were statistically different between those with normal cognitive function and those with aMCI, except for the semantic cue naming of Boston Naming Test (BNT language) scores and the number of errors in Trail Making Test Part A (executive function). Compared to other domains, verbal learning and recall showed stronger relationships with aMCI, of which delayed recall showed the strongest association. This finding is in line with previous studies. Zhao's study found that both short-term delay and long-term delay had the same value in identifying aMCI patients [39]. Fisher's and Simon's study suggested that delayed recall had a higher predictive value for conversion of aMCI to AD compared to other domains of cognitive test [40, 41]. The evidence suggested that the default mode network (DMN), including the posterior cingulate cortex (PCC), medial prefrontal cortex (MPFC), the medial temporal lobe, and the inferior parietal cortex, plays an important role in the encoding and retrieval of plot memory [42–44]. And in people living with mild AD, one of the most prominent characteristics is having problematic connectivity in the DMN[45]. For example, Weiler found that DMN connectivity was related to delayed recall, supporting the hypothesis that DMN plays an important role in episodic memory performance [45].

In our study, we found that increasing age was associated with increased prevalence of aMCI. Age is also the most important factor for AD, with older age being associated with higher rates of AD. In China, a systematic review in 2010 showed that the prevalence of AD was 1.27% at age 65 to 69 years and 18.54% at age 85 to 89 years0[46]. The 2020 Alzheimer's Disease Facts and Figures reported that in the United States, the percentage of people with AD increases greatly with age: 3% of people age 65–74, 17% of people age 75–84 and 32% of people age 85 or older have AD [47]. Similar results were found worldwide. aMCI is a subtype of MCI, is characterized by memory impairment and highly associated with developing into AD. The results of the association between age and prevalence rates of aMCI in different countries are mixed. Many studies reported that age was a risk factor for aMCI [7, 15, 16]. However, Sosa's study in Latin America, China, and India showed while positive relationships between age and aMCI prevalence were seen in some of the countries, others had negative associations [48]. However, age is consistently a risk factor for conversion from aMCI/MCI to AD [49]. It is worth noticing that aMCI is not a normal part of aging, and older age alone is not sufficient to cause aMCI.

A second finding was that education was a protective factor for aMCI. This is consistent with previous studies indicating that increasing education is negatively related to aMCI, MCI, AD, and is also protective against the development of AD [22, 50, 51]. This could be explained by the Cognitive Reserve Hypothesis. To highlight this point, research has shown that having a higher cognitive reserve, which refers to the brain's ability to make flexible and efficient use of cognitive networks (networks of neuron-to-neuron connections), helps a person's ability to cope and compensate for brain damage [47, 52]. Therefore, it is reasonable that having a higher education level can delay the progression of cognitive impairment and AD by way of increasing one's cognitive reserve.

We found that diabetes was a risk factor for aMCI, which is consistent with previous studies. Both cross-sectional and longitudinal studies have demonstrated the effect of diabetes in modulating the risk of cognitive impairment[53–55]. However, the underlying mechanism of how diabetes impairs cognitive function is still unclear. One theory is that cerebral insulin resistance promotes tau protein phosphorylation, which facilitates the brain's susceptibility to neurodegeneration, which in turn may lead to AD disease[56]. Another emerging concept in mechanistic studies is the potential role of advanced glycation end products (AGEs). AGEs increase the production of reactive oxygen species, which promote oxidative stress and inflammatory cytokines, leading to diabetes-associated neurovascular damage[57]. Moreover, diabetes is also associated with abnormalities such as accelerated hippocampal atrophy and decreases in whole brain volume, leading to neurodegeneration[54].

We did not observe an association between hypertension and aMCI after adjusting for demographic factors. Some studies have shown that hypertension was associated with cognitive impairment and dementia [58, 59], however, there is no clear answer on the effects of hypertension on the subtypes of mild cognitive impairment. Casado's study observed that hypertension was associated with aMCI [60], while others found arelationship with naMCI, especially with vascular dementia (VaD)[18, 58]. Moreover, the evidence showed that aMCI had a greater tendency to develop into AD, while naMCI was more likely to develop into VaD [12, 19]. In our study, we did not observe an association bewteen aMCI and cardio-cerebrovascular diseases, smoking, and drinking, which may indicate that cardio-cerebrovascular related diseases and risk factors are not related to aMCI, but instead to naMCI. However, we did not have enough naMCI cases in our study to investigate if hypertension and other cardio-cerebrovascular diseases were related to naMCI. In addition, given that most current studies do not consider the severity or duration of hypertension, there is room to expand our understanding of the mechanism through which hypertension and cardio-cerebrovascular diseases impact aMCI, naMCI, VaD, and AD. This could be further explored with a well-designed cohort study.

Finally, we did not find an association between aMCI and sleep disorders. Although there were many studies which showed that sleep disturbance increased risk of aMCI [61–63], some studies demonstrated the opposite. Gavuoto’s study in a large sample of community-dwelling older adults found that those who had less sleep disruption were more like to report higher levels of subjective memory decline, one of the diagnostic criteria for aMCI [64]. They argued that this might be due to compensatory sleep behavior in response to greater cognitive effort to maintain memory function [64]. It should be noted that the Pittsburgh Sleep Quality Index scale does not have indices of sleep depth and stages, indicating different sleep patterns. Analyzing sleep patterns will also help us to understand which kind of sleep disturbance are associated with aMCI and AD. A system review foundthat patients with aMCI may experience more disturbances in sleep efficiency and slow wave sleep [65]. Further longitudinal analyses of cohorts will be required to fully evaluate the associations between sleep and aMCI.

Strengths And Limitations

By dividing participants with MCI into its clinical subtypes, we were able to explore risk factors for amnestic mild cognitive impairment (aMCI) that had a higher probability to convert into Alzheimer's dementia (AD). These results have great implications for AD prevention. We also compared cognitive characteristics between cognitively normal participants and participants with aMCI. When implicated in clinical practice, our findings suggest clinicians need to pay more attention to patients who have verbal learning and memory problems, especially in long-term delayed recall.

We recognize several important limitations as well. First, although our sample is representative for urban settings, urban settings have a lot of difference from rural settings in terms of economic, culture, and so on. Therefore, our results should not be generalized to rural older adults. Besides, given that community samples are expected to be milder than those of clinical samples, and these results cannot be generalized to clinical samples. Second, even though we used strict criteria to identify aMCI cases, we did not have brain imaging or genetic information, both of which are important for diagnosing aMCI. Thus, the prevalence of aMCI may be slightly overestimated. Finally, this was a cross-sectional study that should not be used to generate causal relationships. To understand the dynamic processes that potentially contribute to the development of aMCI, research with longitudinal designs are needed.

Conclusion

This study found a high prevalence of aMCI in urban, community-dwelling older adults aged 60 years and over in Chengdu, China. Compared with cognitively normal persons, people living with aMCI showed lower cognitive function in memory, language, and executive domains, among which long-term delayed recall had the strongest association with aMCI after adjusting age, gender and education. Therefore, this study suggests that in clinical practice, clinicians should pay more attention to people who have verbal learning and memory problems, especially those with problems in long-term delayed recall. Moreover, this study shows that older age, lower education and diabetes are associated with aMCI. The results indicate that cognitive training and chronic disease management may prevent and delay the development of Alzheimer's dementia.

Abbreviations

MCI: mild cognitive impairment; aMCI: amnestic MCI; MMSE: Mini-Mental State Examination; CDR: Clinical Dementia Rating; AVLT: Auditory Verbal Learning Test; LMT : Wechsler's Logical Memory Task; BNT: Boston Naming Test; TMT-A: Trail Making Test Part A; AD: Alzheimer's Disease; naMCI: non-amnestic MCI; UDS: Uniform Data Set; NACC: National Alzheimer's Coordinating Center; GDP: Gross Domestic Product; GDI-SR: self-reported version geriatric depression inventory; SN: spontaneous naming scores; CN: naming scores after phonemic cue; PSQI: Sleep Quality Index scale; SD: standard deviation; DMN: default mode network; PCC: posterior cingulate cortex; MPFC: medial prefrontal cortex; AGEs: advanced glycation end products.

Declarations

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Author’s contributions

PQ designed the study, carried it out, supervised the data collection and wrote the manuscript. YC designed the study, carried it out, analyzed the data and wrote the manuscript. YYW and SL analyzed the data and assisted with writing the article. YN assisted with writing and critical revision the article. YW and SR contributed to the design and supervised the data collection. WK was responsible for designing the study, carrying it out, supervising the data collection and analysis and revising the manuscript.

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Availability of data and materials

The datasets used during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was reviewed and approved by the Special Committee on Clinical trial and Biomedical Ethics in West China Hospital of Sichuan University. Informed consent was signed by all participants before interviews. All participants were free to ask any questions and to withdraw if they did not wish to continue. All procedures comply with the ethical standards of the relevant national and institutional committees on human experimentation.

Consent for publication

Not applicable.

Conflict of interest

None.

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