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ORIGINAL RESEARCH

Epidemiology and Risk Factors Characteristics of Alzheimer's Disease in Southwestern China: A Cross-Sectional Study

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Video abstract

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Background: To address the regional heterogeneity of Alzheimer's disease, a large-scale epidemiological study of 12,421 elderly individuals was conducted in southwestern China to depict its unique risk characteristics.

Methods: A total of 12,421 subjects were selected via cluster sampling from southwestern China after low quality data were filtered out. On the basis of investigations and medical imaging examinations, three groups were distinguished: the AD, mild cognitive impairment (MCI), and normal control groups. The risk factors for AD and MCI were analysed via a multivariate logistic regression model.

Results: This study identifies a high burden of cognitive impairment in southwestern China, with 22.07% of adults aged ≥60 years exhibiting cognitive decline and 5.81% diagnosed with Alzheimer's disease rates surpassing national and global averages. Key risk factors included age >80 years, female sex, low education, rural residence, surgical history, and urological comorbidities. These findings underscore the need for region-specific prevention strategies, prioritizing older, less-educated rural women through combined cognitive and vascular interventions, while integrating cognitive screening into primary care in underserved areas for early detection and intervention.

Conclusion: Elderly individuals in southwestern China exhibit a high prevalence of cognitive impairment, with AD associated with complex risk factors including established contributors like advanced age, dementia family history, alcohol abuse, and multisystem comorbidities-while notably identifying surgical history and urolithiasis as region specific risk signals. These findings underscore regional, environmental, and ethnic influences on AD pathogenesis, requiring tailored prevention/treatment. Future priorities include integrating brief cognitive screening into primary care, targeting high-risk groups (eg, undereducated rural elderly women), and establishing prospective cohorts to clarify causal links between urolithiasis, surgical history, and cognitive decline for refined region-adapted AD prevention.

Keywords: Alzheimer's disease, MCI, epidemiology, China, risk factor

Background

Dementia refers to a syndrome of chronic, acquired, and progressive cognitive impairment, encompassing various types, including Alzheimer's disease (AD), vascular dementia, frontotemporal dementia, Lewy body dementia, and Parkinson's disease dementia. With the increasing severity of the aging of the global population, the incidence rate of dementia has

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shown a significant upwards trend. Among types of dementia, AD stands out as a major subtype, accounting for more than half of all dementia cases, warranting particular attention.[1,2] Mild cognitive impairment (MCI) is a state of cognitive decline that is not directly classified as dementia. It may either return to normal or progress to AD over time, depending on environmental and other factors. Individuals with MCI are then crucial groups to be noted. Since prevention and intervention strategies differ among various types of cognitive impairments, conducting epidemiological surveys to provide information on risk factors, distribution patterns, and even pathological characteristics is essential. Such insights are highly important for further in-depth research into AD and for enhancing its prevention, control, and treatment strategies.

Previous studies have indicated that age, sex, and educational attainment are significant risk factors for AD.[3] Other studies have also identified associations between AD incidence and factors such as race, lifestyle, and underlying health conditions.[4] However, given that the fundamental pathogenesis remains unresolved, it is pivotal to observe and analyse these risk factors dynamically in AD prevention and treatment. The Alzheimer's Association of America reported that an estimated 6.7 million Americans suffered from Alzheimer's disease in 2023, representing approximately 2% of the population in the United States.[5] This report highlights the importance of comprehensive data encompassing different races and ethnicities.[5] Owing to differences in genetic polymorphisms, cultural backgrounds, and lifestyles, the prevalence characteristics of dementia show certain disparities between Eastern and Western populations.[6] A recent authoritative survey in China revealed that the incidence rate of dementia is approximately 6.0% among the 1.4 billion population, with AD accounting for 3.9% (54.6 million).[7] A comparison between patients from China and those from the United States highlights the influences of race, environment, and lifestyle on dementia.[8] Given the large population and diverse ethnic composition in China, along with significant differences in natural environments, lifestyles, and economic levels between the eastern and western regions, previous studies have shown that the prevalence of AD varies considerably across different regions within China.[9]

The southwestern region of China has a total population of approximately 285 million, accounting for approximately 23% of the national population and over 50% of the population in the western region. For geographical and historical reasons, the southwestern region is characterized by large linguistic differences among multiple ethnic groups, limited educational attainment due to historically poor information access, and relatively underdeveloped economic conditions that impact the diagnosis and treatment of underlying diseases. This study aims to reveal the impact of region-specific factors including ethnicity, socioeconomic status, and healthcare accessibility on Alzheimer's disease by comparing the discrepancies in the AD prevalence rate in Southwest China with national and global average levels. It further seeks to provide a scientific basis for the early intervention of high-risk groups and the optimal allocation of medical resources in this region, as well as to offer key localized data support for formulating differentiated public health policies for cognitive health and refining health service models in multi-ethnic regions.

Methods

Study Design (Materials and Methods)

This project was initiated by Guizhou University, the Affiliated Hospital of Zunyi Medical University, and the Guizhou Alzheimer's Disease Prevention and Treatment Association. This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Affiliated Hospital of Zunyi Medical University (KLL-2022-460). Registration was completed at the China Clinical Trial Center on June 3, 2022 (ChiCTR2200060465; https://www.chictr.org.cn/). The study was conducted after informed consent was obtained from the study participants or their guardians. Reason for guardian signatures: Informed consent was obtained from legal guardians for participants belonging to two distinct categories: (1) individuals who were illiterate and unable to provide a signature, and (2) individuals with moderate to severe cognitive impairment who lacked the capacity to independently sign the informed consent form. Therefore, guardians signed the consent forms for participants in these two categories. The research employed a method of regional stratification, cluster sampling, and stratified screening. The study was conducted from June 2022 to May 2024 across nine cities/counties and 24 townships in three provinces or municipalities in southwestern China, including Sichuan, Chongqing, and Guizhou. Regional stratification was divided into two levels: the first level

consisted of medium-sized cities/counties with populations ranging from 500,000 to 2.5 million, where community-based recruitment was used for the survey. The second level consisted of townships with populations of less than 100,000, where surveys were conducted through centralized community outreach or door-to-door visits. These two levels of stratification involve differences in economic conditions and cultural backgrounds. The study targeted elderly individuals aged 60 years and above for cluster sampling. After sampling, primary screening classified participants into three groups: those with mild cognitive impairment (MCI), those with suspected AD, and those with other types of dementia. Participants in the suspected AD group underwent medical imaging examinations. Those diagnosed with AD after excluding cerebrovascular and organic brain lesions through imaging completed the secondary screening, refining the identification of AD cases. Finally, the secondary screening results, combined with basic demographic information, medical data, and scale scores, were used to analyse the prevalence characteristics and risk factors for AD.

The sample size was calculated using the formula for cross-sectional studies: $n=\frac{z^2_{1-\alpha/2}\times P\times(1-P)}{d^2}$ The parameters were set as follows: a confidence level of 95% (Z=1.96) and a margin of error (d) of 0.01. Given that literature reports the prevalence of Alzheimer's disease in the local region to be between 5% and 12%, the upper value of P=12% was used to ensure an adequate sample size. This calculation yielded an initial sample size of 4054 individuals. Further accounting for an anticipated 15% non-response rate and a design effect of 1.5, the final required sample size was determined to be 6080 older adults. Missing or incomplete data will not be considered valid data and will not be included in the final statistics.

Research Team Composition, Division of Labor, and Quality Control System

The expert group is composed of one senior neuropsychological consultant responsible for mental health guidance, one senior neurologist responsible for professional diagnostic training and guidance, and one senior neurologist with basic psychological assessment qualifications who acts as the quality control officer. The investigation team includes one senior clinician serving as the project implementation commander and emergency event manager, one nurse responsible for blood sample collection, and four medical personnel with basic psychological assessment qualifications who collect data for the case report form (CRF), including one liaison officer. Two senior radiologists performed medical imaging diagnostics. In regions involving minority languages, one doctor will be trained as a translator, and a local social worker will be recruited to assist with data collection. Before project implementation, a one-day specialized training session and a simulated practice assessment will be conducted. Those who fail the assessment will undergo retraining until they meet the consistency standards for data collection. The quality control officer performs initial quality checks on the first CRF collected by each data collector and on the first report by each radiologist. Subsequent quality checks involve random inspections of no fewer than five cases after the completion of work at each collection site. Feedback, corrections, and improvements will be provided to the research team after each quality control review. The entire team will undergo collective training every six months. All CRF data will ultimately be entered into an electronic case report form (ECRF) and securely stored by the designated data custodian.

Evaluation System and Diagnostic Criteria

In the initial screening, all participants who received a clinical dementia rating (CDR) of 0 were preliminarily classified as having normal cognitive function.

Cognitive Function Preliminary Screening Evaluation System

Step 1: Basic information is collected to identify individuals aged 60 years and above. The CDR, Montreal Cognitive Assessment (MoCA) scales are used to determine the presence of cognitive impairment. Those who meet the criteria proceed to the second step of evaluation.

Step 2: Medical history is collected, and the Activities of Daily Living (ADL) and Hachinski Ischemic Scale are used to assess the possibility of cerebrovascular and organic brain lesions.

On the basis of the results of these evaluations and referencing the diagnostic criteria for mild cognitive impairment (MCI) and Alzheimer's disease (AD), participants from the initial screening were categorized into three groups: MCI, suspected AD, and other types of dementia.

AD Secondary Screening Evaluation System

For the group initially screened for AD, simple random sampling is employed for further evaluation. Participants undergo cranial CT/MRI scans, and the results are combined with AD imaging diagnostic criteria to definitively classify individuals as having either confirmed AD or other types of dementia.

MCI Diagnostic Criteria

The diagnosis of dementia is based on the criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR). According to the 2018 Chinese Guidelines for the Diagnosis and Treatment of Dementia and Cognitive Impairment (V): Diagnosis and Treatment of Mild Cognitive Impairment, it is recommended that MCI be diagnosed following these international standards.

AD Diagnostic Criteria

The diagnosis of Alzheimer's disease is based on the criteria established by the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the Alzheimer's Disease and Related Disorders Association (ADRDA) or the criteria set by the National Institute on Ageing and the Alzheimer's Association (NIA-AA) workgroup. Vascular dementia is diagnosed according to the criteria of the National Institute of Neurological Disorders and Stroke-Association Internationale pour la Recherche et l'Enseignement en Neurosciences (NINDS-AIREN).

According to the clinical standards recommended by the NIA-AA workgroup, participants who exhibit cognitive abnormalities but do not meet the criteria for dementia are classified as having mild cognitive impairment (MCI). The diagnostic criteria for AD using cranial CT/MRI include indicators such as changes in brain volume (eg, hippocampal or medial temporal lobe atrophy), white matter lesions, or gray matter lesions but exclude other types of organic brain lesions.

Primary Screening

Elderly individuals aged 60 years and above within the survey area were selected as the primary study population. In urban communities, the residents' committees conducted recruitment one week in advance, followed by centralized surveys at designated locations. In townships, local community committees also recruited participants one week prior, with surveys conducted either through centralized methods or door-to-door visits during the survey period. All participants were accompanied by their guardians and engaged with researchers in open, independent spaces.

Inclusion Criteria

1. The actual age was ≥ 60 years, with no sex restrictions.
2. Conscious and alert.
3. Stable vital signs.

The participants or guardians voluntarily signed the informed consent form and agreed to cooperate with the study.

Exclusion Criteria

1. Individuals with underlying conditions such as deafness, muteness, blindness, or congenital intellectual disabilities that prevent completion of scale tests.
2. Those who have undergone scale testing and training within the past month.
3. Participants who speak only minority languages that cannot be adequately translated for testing.
4. Individuals with severe psychiatric disorders.
5. Those with serious illnesses that may pose a life-threatening risk during the study.
6. Any situation deemed inappropriate by the researchers for inclusion in the study (eg, intentional disruption of the research process, making unreasonable demands, threatening the researchers, etc).

Exclusion Criteria

1. Individuals who, for any reason, fail to complete data collection.
2. Those who repeatedly interrupt the researcher's questions or seek assistance from others during scale testing.
3. Participants who were unwilling to continue cooperating during the study.

AD Secondary Screening

Participants initially screened and identified as having suspected AD, MCI, or other types of dementia underwent cranial CT/MRI examinations for further secondary screening.

Inclusion Criteria

1. Participants were diagnosed with suspected AD or other types of dementia during the primary screening.
2. Participants for whom MCI or other dementias could not be definitively classified during the primary screening.
3. Participants who voluntarily agreed to undergo and cooperate with cranial CT/MRI examinations.

Exclusion Criteria

1. Individuals with a history of psychological trauma, schizophrenia, Parkinson's disease, or prion disease.
2. Individuals with a history of severe brain tumors, epilepsy, or moderate to severe demyelinating brain lesions.
3. Individuals with a history of severe head trauma, infections, or poisoning.
4. Individuals with a confirmed history of severe cerebral hypoxia.
5. Individuals with nutritional deficiency-related encephalopathy.
6. Individuals with focal neurological damage characteristics or extrapyramidal system lesions.
7. Individuals with confirmed neurofunctional impairments caused by endocrine or metabolic systemic diseases.
8. Individuals on long-term medication with hormones or immunosuppressants.
9. Any situation deemed inappropriate by the researchers for continued inclusion in the screening process.

Exclusion Criteria

1. Inability to obtain imaging results for any reason.
2. Imaging results that exceed the diagnostic criteria for AD and include other types of organic brain lesions.
3. Incomplete screening due to unforeseeable emergency events (eg, fire, earthquake, equipment failure).

Investigation Indicators

Basic information: Name, sex, age, ethnicity, family history, place of residence, years of education, cohabitation status, nature of employment, smoking history, and alcohol abuse history.

Medical information: Surgical history; comorbidities across various systems (nervous system, cerebrovascular system, cardiovascular system, respiratory system, endocrine system, urinary system, and digestive system); sleep–wake duration; sleep duration; and emotional status.

Explanation of Medical Information

Surgical history: 0 operations, 1 operation, >1 operation

Sleep–wake duration (weekly nighttime sleep–wake duration): >3 hours, 1–3 hours, <1 hour

Sleep duration: <4 hours, 4–8 hours, >8 hours

Emotional status: Emotionally stable, apathetic, and irritable.

Scale Scores

Clinical Dementia Rating (CDR)

Montreal Cognitive Assessment (MoCA)

Activity of Daily Living Scale (ADL)

Hachinski Ischemic Score (used to differentiate AD from vascular dementia).

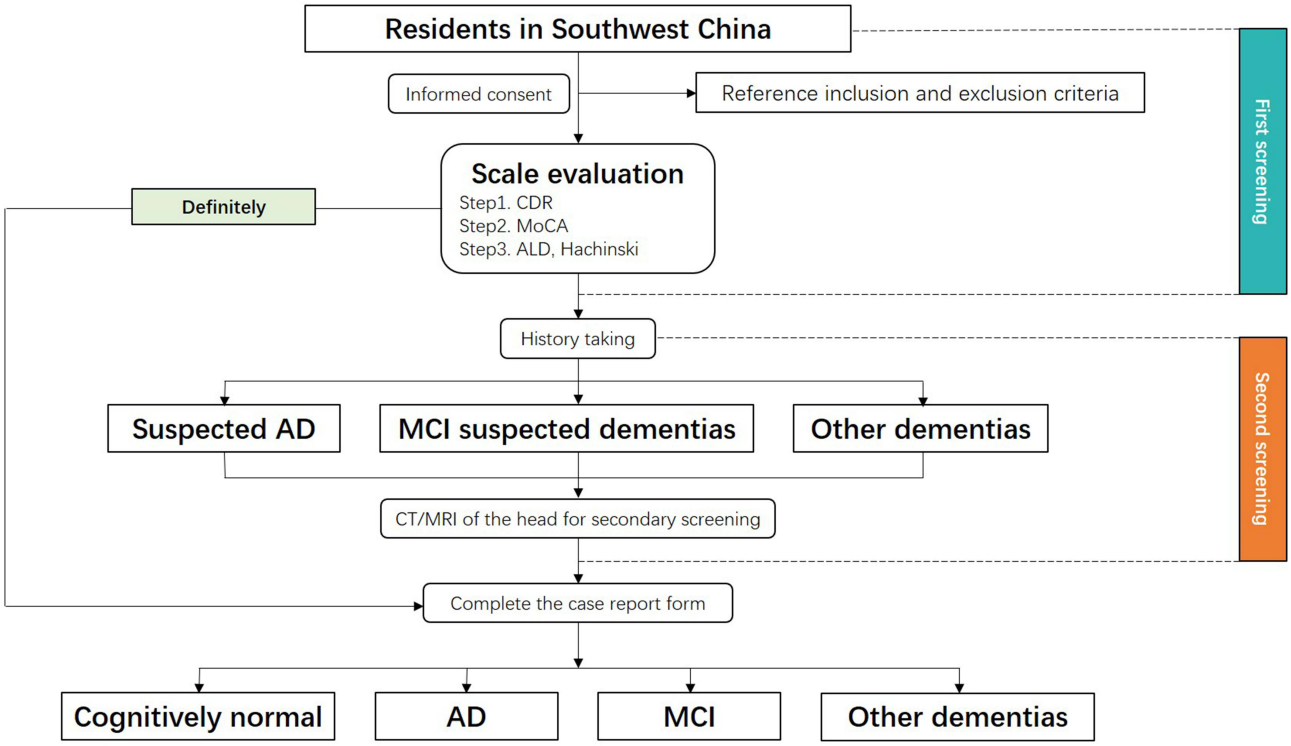

Figure 1 Survey procedure.

Statistical Analysis

Statistical analyses were conducted via Stata software (version 13.0). For quantitative data, if the data followed a normal distribution, the mean and standard deviation were used for descriptive statistics. For data that did not follow a normal distribution, the median and interquartile range were calculated. For categorical variables, frequencies and percentages were used for descriptive statistics. Unconditional logistic regression models were applied for univariate and multivariate analyses. All tests were two-sided, and $p<0.05$ was considered statistically significant as shown in Figure 1.

Results

Overall Profiles

This study included a total of 16,537 participants from the southwestern regions of China, specifically Sichuan and Guizhou Provinces and Chongqing municipality. In Sichuan Province, surveys were completed with 3132 participants across three cities, including 11 urban communities (1651 participants) and 14 rural communities (1481 participants). In Chongqing municipality, surveys were completed with 3875 participants across three cities, including 12 urban communities (1846 participants) and 14 rural communities (2029 participants). In Guizhou Province, surveys were completed with 5414 participants across three cities, including 21 urban communities (2615 participants) and 14 rural communities (2799 participants).

Exclusions were made for participants for various reasons, including visual or hearing impairments (713 participants), incomplete data collection (2668 participants), seeking help from others during the study (426 participants), refusal to undergo imaging examinations (264 participants), inability to cooperate with imaging examinations (37 participants), and detection of complex organic brain lesions during imaging (8 participants). Finally, 4116 participants were removed from the datasets, and a sample size of 12,421 participants was obtained after these exclusions.

After filtering, 9680 participants were classified into the control group with normal cognitive functions (4917 males, 4763 females), 722 persons were diagnosed with AD (294 males, 428 females), 1920 participants were diagnosed with MCI (847 males, 1073 females), and 99 people were identified as having other types of dementia (62 males, 37 females) (Figure 2).

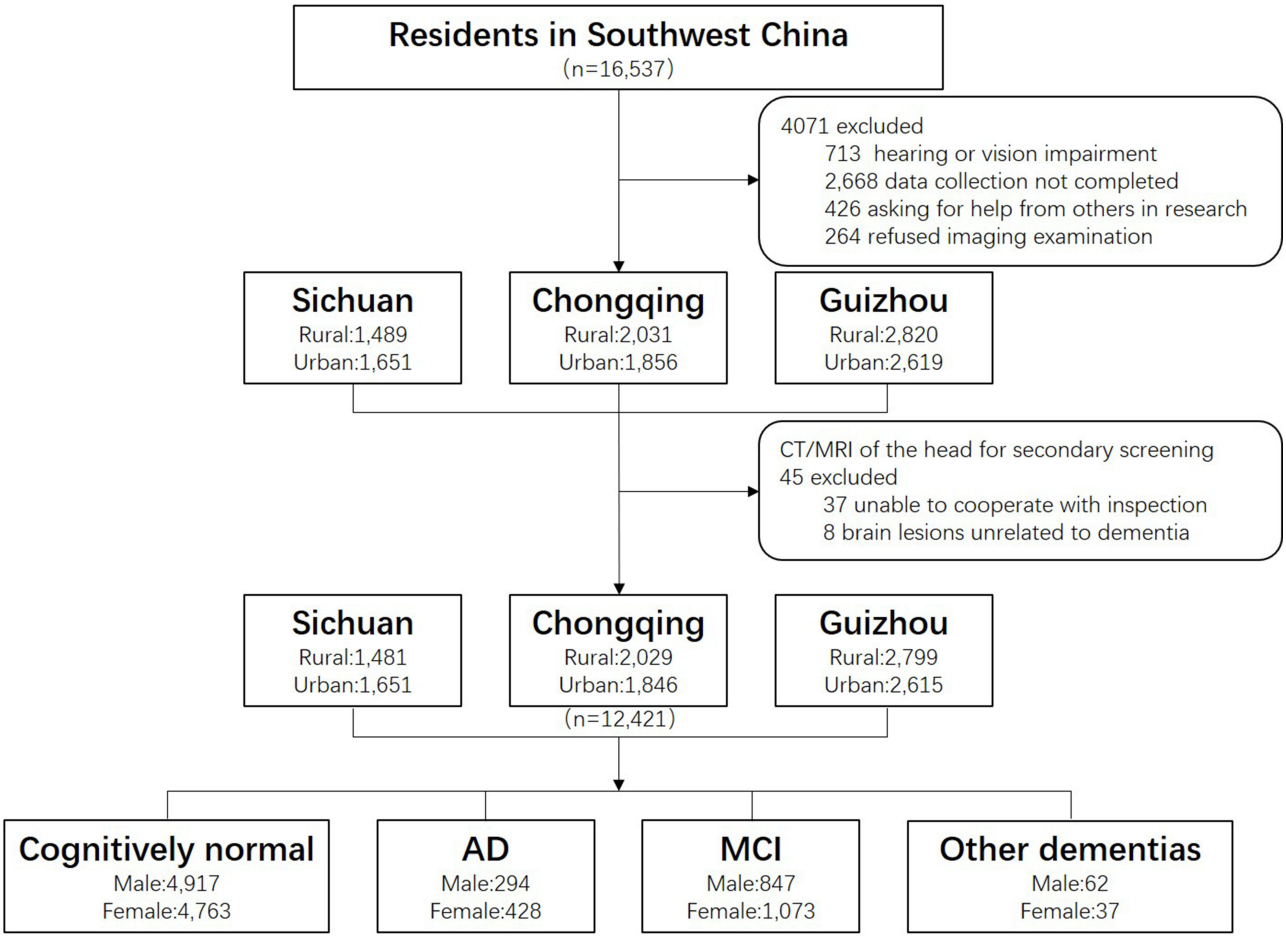

Figure 2 Sample selection process and classification.

Differences Between Normal Cognitive and Cognitive Dysfunction

Following the screening process, the study population was first divided into two categories: those with normal cognitive function and those with cognitive decline. The subjects with varying degrees of cognitive decline accounted for 22.07% of the total surveyed population. The sampling process ensured consistency in terms of gender distribution (49.27% male and 50.73% female) and urban–rural residence (49.21% urban and 50.79% rural). Among those aged 60 years and above, the illiteracy rate was 27.48%, and 61.06% were engaged in manual labor. Cardiovascular diseases were the most common comorbidity among the elderly in this region, affecting 40.30% of the total population. A comparison of basic and medical information between the two groups revealed statistically significant differences in all variables except for smoking and alcohol consumption (Table 1). Individuals with cognitive decline presented markedly abnormal scores across all assessment scale scores (Figure 3).

Risk Factors for AD and MCI

On the basis of their cognitive levels, 722 individuals with AD (5.81%), 1920 individuals with MCI (15.46%), and 99 individuals with other types of dementia (0.80%) were diagnosed with three types of cognitive dysfunction. Other types of dementia samples were small and not analysed. Using the normal group as the reference, univariate logistic regression analysis was performed on various indicators for the remaining two groups (Table 2).

The basic information revealed that females were significantly more likely to be diagnosed with AD (OR 1.50 [95% CI 1.29–1.75]) and MCI (OR 1.31 [95% CI 1.19–1.44]) than males were. The difference between the 70–79 age groups in the AD group and the normal group was not significant (OR 0.88 [95% CI 0.72–1.07]); however, a significant

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Table 1 Comparison of Indicators Between the Cognitive Dysfunction Group and the Normal Cognitive Group

	All Population (n=12,421)	Normal Cognitive (n=9680)	Cognitive Dysfunction (n=2741)	Chi Square	*p* value
Incidence		77.93%	22.07%		
Sex				40.76	<0.001
Male	6120(49.27)	4917(50.80)	1203(43.89)		
Female	6301(50.73)	4763(49.20)	1538(56.11)		
Age group(year)				266.73	<0.001
60-69	2775(22.34)	2456(25.37)	319(11.63)		
70-79	7894(63.55)	5997(61.95)	1897(69.22)		
>80	1752(14.11)	1227(12.68)	525(19.15)		
Ethnic groups				105.72	<0.001
Han nationality	11251(90.58)	8907(92.01)	2344(85.52)		
Ethnic minorities	1170(9.42)	773(7.99)	397(14.48)		
Parental history of dementia				556.04	<0.001
No	8655(69.68)	7215(74.54)	1440(52.54)		
Yes	554(4.46)	289(2.99)	265(09.67)		
Unknown	3212(25.86)	2176(22.47)	1036(37.79)		
Residence location				75.85	<0.001
Urban	6309(50.79)	5118(52.87)	1191(43.45)		
Rural	6112(49.21)	4562(47.13)	1550(56.55)		
Education level(year)				372.94	<0.001
<1	3413(27.48)	2288(23.64)	1125(41.04)		
1-3	1274(10.26)	996(10.29)	278(11.29)		
4-6	1966(15.83)	1720(17.77)	246(08.98)		
>6	5768(46.43)	4676(48.30)	1092(38.69)		
Live together				556.04	<0.001
Live alone	680(5.47)	309(3.19)	371(13.54)		
Husband and wife	8582(69.09)	7074(73.08)	1508(55.01)		
Children and children	2466(19.86)	1973(20.38)	493(17.99)		
Other	693(5.58)	324(3.35)	369(13.46)		
Occupation				36.94	<0.001
Manual labor	7584(61.06)	6001(61.99)	1583(57.75)		
Mental work	2021(16.27)	1602(16.55)	419(15.29)		
Unemployed/other	2816(22.67)	2077(21.46)	739(26.96)		
Current smoker				1.637	0.201
No	9746(78.46)	7571(78.21)	2175(79.35)		
Yes	2675(21.54)	2109(21.79)	566(20.65)		
Current drinking				0.393	0.531
No	11806(95.06)	9196(95.00)	2610(95.29)		
Yes	613(4.94)	484(5.00)	129(04.71)		
Nervous system diseases				793.74	<0.001
No	11900(95.81)	9535(98.50)	2365(86.28)		
Yes	521(4.19)	145(1.50)	376(13.72)		
Cerebrovascular disease				673.93	<0.001
No	12042(96.95)	9591(99.08)	2451(89.42)		
Yes	379(3.05)	89(0.92)	290(10.58)		
Cardiovascular diseases				85.24	<0.001
No	7415(59.70)	5988(61.86)	1427(52.06)		
Yes	5006(40.30)	3692(38.14)	1314(47.94)		

(*Continued*)

Table 1 (Continued).

	All Population (n=12,421)	Normal Cognitive (n=9680)	Cognitive Dysfunction (n=2741)	Chi Square	*p* value
Respiratory diseases				1070.17	<0.001
No	11618(93.54)	9426(97.38)	2192(79.97)		
Yes	803(6.46)	254(2.62)	549(20.03)		
Endocrine system diseases				69.76	<0.001
No	10466(84.26)	8297(85.71)	2169(79.13)		
Yes	1955(15.74)	1383(14.29)	572(20.87)		
Urinary system diseases				348.88	<0.001
No	11759(94.67)	9358(96.67)	2401(87.60)		
Yes	662(5.33)	322(3.33)	340(12.40)		
Digestive system diseases				32.75	<0.001
No	10702(86.16)	8249(85.22)	2453(89.49)		
Yes	1719(13.84)	1431(14.78)	288(10.51)		
Emotion				682.19	<0.001
Stability	11564(93.10)	9318(96.26)	2246(81.94)		
Indifferent	618(4.98)	258(2.67)	360(13.13)		
Irritable	239(1.92)	104(1.07)	135(04.93)		
Surgical history				402.44	<0.001
None	8573(69.02)	7012(72.44)	1561(56.95)		
1	3438(27.68)	2485(25.67)	953(34.77)		
>1	410(3.30)	183(1.89)	227(08.28)		
Sleep awakening time				342.7	<0.001
>3 h	1908(15.36)	1610(16.63)	298(10.87)		
1-3 h	6961(56.04)	5002(51.67)	1959(71.47)		
<1 h	3552(28.60)	3068(31.70)	484(17.66)		
Sleep duration				439.84	<0.001
<4 h	254(2.04)	77(0.80)	177(06.46)		
4-8 h	6976(56.17)	5282(54.56)	1694(61.80)		
>8 h	5191(41.79)	4321(44.64)	870(31.74)		

Note: Data are n (%) or mean (SD) unless specified otherwise.

difference emerged in AD individuals aged over 80 years (OR 2.92 [95% CI 2.36–3.62]). For MCI patients, the risk also increased with age. Statistically significant differences were found between the AD and MCI groups and the normal cognitive function group in terms of ethnicity, family history of disease, rural residence, illiteracy, and manual labor ($p<0.05$). However, the impact of cohabitation status differed between the AD and MCI groups ($p>0.05$).

In terms of medical information, emotional changes were significantly different between the AD and MCI groups and the normal cognitive function group. Gastrointestinal comorbidities were not significant in the AD group ($p>0.05$) but were statistically significant in the MCI group (OR 0.60 [95% CI 0.51–0.70]). Other comorbidities were significantly different between the AD and MCI groups. The difference in sleep–wake duration was not significant between the AD group and the normal group; however, a sleep–wake duration of 1–3 hours was significantly associated with MCI (OR 3.11 [95% CI 2.62–3.70], $p<0.001$) compared with the normal group.

The scale scores revealed no statistically significant difference between the AD group and the other types of dementia in terms of the CDR and MoCA scores ($p>0.05$). However, significant differences were found between the other groups ($p<0.001$). There were also significant differences among all groups in ADL, and Hachinski scores ($p<0.001$) (Figure 4).

Further multivariate logistic regression analysis was conducted for the AD and MCI groups (Table 3). For the AD group, the analysis of basic information indicated that females, rural residents, individuals with low educational

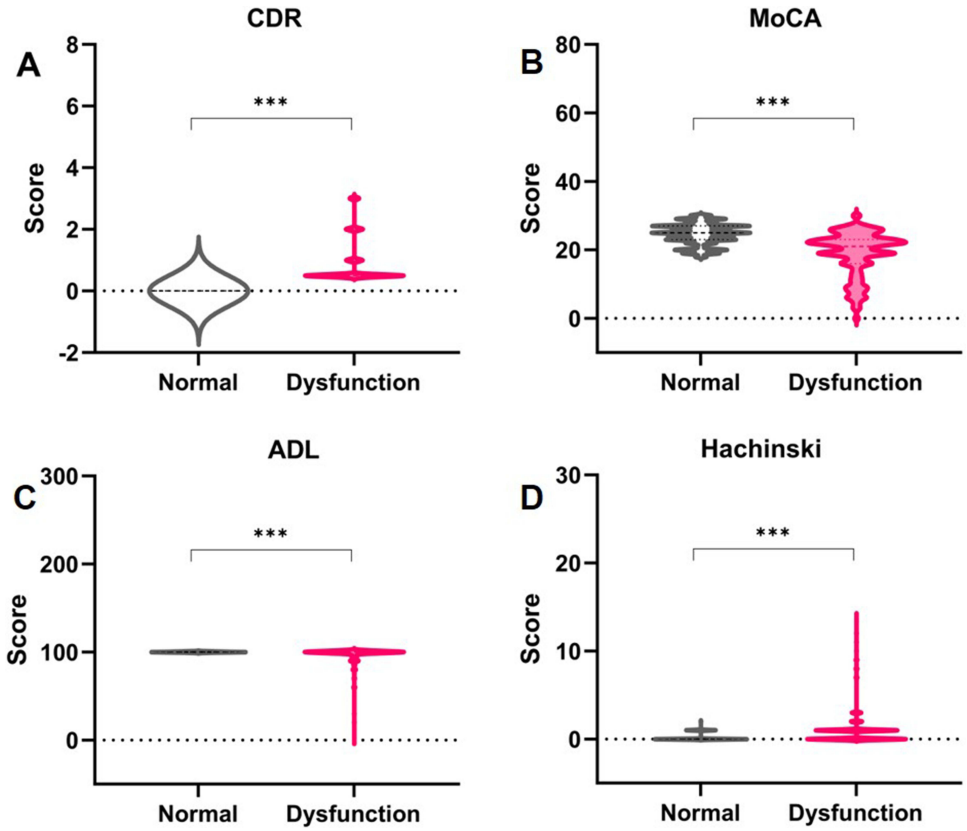

Figure 3 Comparison of score scales between groups with normal cognitive function and those with decreased cognitive function. (**A**) CDR score. (**B**) MoCA score. (**C**) ADL score. (**D**) Hachinski score. ***: $p<0.001$.

attainment, and manual laborers were identified as high-risk factors ($p<0.05$). The risk of developing AD increased significantly after the age of 80 years (OR 2.51 [1.88–3.35], $p<0.001$). A parental history of dementia (OR 3.60 [2.41–5.38], $p<0.001$) and a history of alcohol abuse (OR 2.41 [1.57–3.69], $p<0.001$) were identified as risk factors for AD. The medical information in the AD group revealed that emotional apathy and irritability were significant risk factors, as were a history of surgeries and the number of surgeries undergone. With the exception of gastrointestinal comorbidities ($p<0.001$), all other system comorbidities were found to be risk factors. Additionally, short sleep duration was identified as an important risk factor ($p<0.001$). We further analysed the risk factors for the MCI group because AD patients might have come from MCI patients. These findings indicated that age was a significant risk factor ($p<0.001$). Ethnic minorities, a family history of dementia, lower educational attainment, cohabitation status, and manual laborers were also identified as high-risk groups ($p<0.001$). The medical information for the MCI group revealed that emotional apathy and irritability were risk factors, as were a history of surgery and the number of surgeries undergone ($p<0.001$). Comorbidities of the nervous system, circulatory system, respiratory system, urinary system, and digestive system were identified as risk factors ($p<0.001$). Additionally, short sleep duration was highlighted as an important risk factor ($p<0.001$).

Among the total analyzed population (N=12,421), the prevalence of Alzheimer's disease (AD) was 5.81% (722/12,421; 95% CI: 5.41–6.21%), and that of mild cognitive impairment (MCI) was 15.46% (1920/12,421; 95% CI: 14.83–16.09%). This substantial sample size yielded precise prevalence estimates, as indicated by the narrow confidence intervals.

In multivariate logistic regression models adjusted for age and sex, both variables were identified as independent risk factors. The odds of AD increased significantly in individuals aged over 80 years (adjusted OR: 2.51, 95% CI:

Table 2 Univariate Logistic Analysis Among Groups

	Normal Cognitive (n=9680)	AD (n=722)	Univariable OR (95% CI)	*p* value	MCI (n= 1920)	Univariable OR (95% CI)	*p* value
Prevalence		5.81%			15.46%		
Sex							
Male	4917(50.80)	294(40.72)	1.00		847(44.11)	1.00	
Female	4763(49.20)	428(59.28)	1.50(1.29–1.75)	<0.001	1073(55.89)	1.31(1.19–1.44)	<0.001
Age group(year)							
60-69	2456(25.37)	157(21.75)	1.00		120(6.25)	1.00	
70-79	5997(61.95)	336(46.54)	0.88(0.72–1.07)	0.186	1512(78.75)	5.16(4.26–6.25)	<0.001
>80	1227(12.68)	229(31.72)	2.92(2.36–3.62)	<0.001	288(15.00)	4.80(3.84–6.01)	<0.001
Ethnic groups							
Han nationality	8907(92.01)	625(86.57)	1.00		1623(84.53)	1.00	
Ethnic minorities	773(7.99)	97(13.43)	1.79(1.43–2.24)	<0.001	297(15.47)	2.11(1.83–2.43)	<0.001
Parental history of dementia							
No	7215(74.54)	410(56.79)	1.00		997(51.93)	1.00	
Yes	289(2.99)	88(12.19)	5.36(4.14–6.94)	<0.001	175(9.11)	4.38(3.59–5.35)	<0.001
Unknown	2176(22.48)	224(31.02)	1.81(1.53–2.15)	<0.001	748(38.96)	2.49(2.24–2.77)	<0.001
Residence location							
Urban	5118(52.87)	257(35.60)	1.00		891(46.41)	1.00	
Rural	4562(47.13)	465(64.40)	2.03(1.73–2.38)	<0.001	1029(53.59)	1.30(1.17–1.43)	<0.001
Education level, year							
<1	2288(23.64)	208(28.81)	1.00		899(46.82)	1.00	
1-3	996(10.29)	124(17.17)	1.37(1.08–1.73)	0.009	148(7.71)	0.38(0.31–0.46)	<0.001
4-6	1720(17.77)	121(16.76)	0.77(0.61–0.98)	0.031	101(5.26)	0.15(0.12–0.19)	<0.001
>6	4676(48.31)	269(37.26)	0.63(0.52–0.76)	<0.001	772(40.21)	0.42(0.38–0.47)	<0.001
Live together							
Live alone	309(3.19)	18(2.49)	1.00		353(18.39)	1.00	
Husband and wife	7074(73.08)	355(49.17)	0.86(0.53–1.40)	0.549	1117(58.18)	0.14(0.12–0.16)	<0.001
Children and children	1973(20.38)	172(23.82)	1.50(0.91–2.47)	0.114	297(15.47)	0.13(0.11–0.16)	<0.001
Other	324(3.35)	177(24.52)	9.38(5.64–15.61)	<0.001	153(7.97)	0.41(0.32–0.53)	<0.001
Occupation							
Manual labor	6001(61.99)	569(78.81)	1.00		992(51.67)	1.00	
Mental work	1602(16.55)	69(9.56)	0.45(0.35–0.59)	<0.001	336(17.50)	1.27(1.11–1.45)	<0.001
Unemployed/other	2077(21.46)	84(11.63)	0.43(0.34–0.54)	<0.001	592(30.83)	1.72(1.54–1.93)	<0.001
Current smoker							
No	7571(78.21)	559(77.42)	–	–	1531(79.74)	–	–
Yes	2109(21.79)	163(22.58)	–	–	389(20.26)	–	–
Current drinking							
No	9196(95.00)	664(92.22)	1.00		1847(96.20)	1.00	
Yes	484(5.00)	56(7.78)	1.60(1.20–2.14)	<0.001	73(3.80)	0.75(0.58–0.97)	0.025
Nervous system diseases							
No	9535(98.50)	490(67.87)	1.00		1824(95.00)	1.00	
Yes	145(1.50)	232(32.13)	31.13(24.82–39.05)	<0.001	96(5.00)	3.46(2.66–4.50)	<0.001
Cerebrovascular disease							
No	9591(99.08)	514(71.19)	1.00		1859(96.82)	1.00	
Yes	89(0.92)	208(28.81)	43.61(33.50–56.76)	<0.001	61(3.18)	3.54(2.54–4.92)	<0.001
Cardiovascular diseases							
No	5988(61.86)	306(42.38)	1.00		1048(54.58)	1.00	
Yes	3692(38.14)	416(57.62)	2.20(1.89–2.57)	<0.001	872(45.42)	1.35(1.22–1.49)	<0.001
Respiratory diseases							
No	9426(97.38)	611(84.63)	1.00		1483(77.24)	1.00	
Yes	254(2.62)	111(15.37)	6.74(5.32–8.55)	<0.001	437(22.76)	10.94(9.28–12.88)	<0.001
Endocrine system diseases							
No	8297(85.71)	511(70.78)	1.00		1567(81.61)	1.00	
Yes	1383(14.29)	211(29.22)	2.48(2.09–2.94)	<0.001	353(18.39)	1.35(1.19–1.54)	<0.001

(*Continued*)

Table 2 (Continued).

	Normal Cognitive (n=9680)	AD (n=722)	Univariable OR (95% CI)	*p* value	MCI (n= 1920)	Univariable OR (95% CI)	*p* value
Urinary system diseases							
No	9358(96.67)	552(76.45)	1.00		1752(91.25)	1.00	
Yes	322(3.33)	170(23.55)	8.95(7.29–10.98)	<0.001	168(8.75)	2.79(2.30–3.38)	<0.001
Digestive system diseases							
No	8249(85.22)	620(85.87)	1.00		1740(90.63)	1.00	
Yes	1431(14.78)	102(14.13)	0.95(0.76–1.18)	0.632	180(9.38)	0.60(0.51–0.70)	<0.001
Emotion							
Stability	9318(96.26)	651(90.17)	1.00		1552(80.83)	1.00	
Indifferent	258(2.67)	44(6.09)	2.44(1.76–3.39)	<0.001	270(14.06)	6.28(5.25–7.51)	<0.001
Irritable	104(1.07)	27(3.74)	3.72(2.42–5.72)	<0.001	98(5.10)	5.66(4.27–7.49)	<0.001
Surgical history							
None	7012(72.44)	276(38.23)	1.00		1216(63.33)	1.00	
1	2485(25.67)	284(39.34)	2.90(2.45–3.45)	<0.001	646(33.65)	1.50(1.35–1.67)	<0.001
>1	183(1.89)	162(22.44)	22.49(17.63–28.68)	<0.001	58(3.02)	1.83(1.35–2.47)	<0.001
Sleep awakening time							
>3 h	1610(16.63)	114(15.79)	1.00		157(8.18)	1.00	
1-3 h	5002(51.67)	408(56.51)	1.15(0.93–1.43)	0.197	1518(79.06)	3.11(2.62–3.70)	<0.001
<1 h	3068(31.69)	200(27.70)	0.92(0.73–1.17)	0.496	245(12.76)	0.82(0.66–1.01)	0.061
Sleep duration							
<4 h	77(0.80)	93(12.88)	1.00		83(4.32)	1.00	
4-8 h	5282(54.57)	366(50.69)	0.06(0.04–0.08)	<0.001	1268(66.04)	0.22(0.16–0.31)	<0.001
>8 h	4321(44.64)	263(36.43)	0.05(0.04–0.07)	<0.001	569(29.64)	0.12(0.09–0.17)	<0.001

Note: Data are n (%) or mean (SD) unless specified otherwise.

1.88–3.35). Furthermore, female gender was associated with higher odds of both AD (adjusted OR: 1.50, 95% CI: 1.29–1.75) and MCI (adjusted OR: 1.31, 95% CI: 1.19–1.44).

Discussion

AD is a heterogeneous disorder influenced by variations in region, ethnicity, culture, and lifestyle.[10] Research across different regions is essential to uncover the commonalities and specificity at the onset and following progression of AD, which would contribute to more effective prevention and treatment strategies. The overall findings of this study indicate that 22.07% of the elderly population aged 60 years and above in southwestern China exhibit cognitive decline, with 5.81% diagnosed with AD, 15.46% with MCI, and 0.80% with other types of dementia. Owing to factors such as limited mobility and caregiver resistance, the actual prevalence of dementia might be greater. These rates are notably higher than both the national average in China and the global average.[7] The western region of China, characterized by mountainous terrain and diverse ethnic populations, was historically impoverished with extremely underdeveloped transportation infrastructure during the mid-20th century. This led to inadequate education and resource scarcity, with many individuals lacking access to systematic and high-quality education in their early years. These conditions are similar to those in certain underdeveloped regions worldwide today. The limitations imposed by such conditions may have led to insufficient stimulation of learning and memory abilities during childhood, accelerating cognitive decline as these individuals aged, thereby contributing to the increased prevalence of cognitive impairment observed in this study. This trend is also reflected in the finding that AD incidence is significantly higher in rural areas than in urban areas. The majority of rural residents are engaged in manual labor, and the prevalence of AD is greater among these individuals than among those engaged in mental labor. This observation aligns with the suggestion of Chen et al[11] that enhancing the cognitive reserve in the elderly population in rural China is crucial for improving their cognitive health.[11] Previous studies have discussed the relationship between training in learning and memory abilities during youth and the long-term risk of cognitive impairment.[12] Emerging memory training methods, such as digital applications and video games, have been shown to

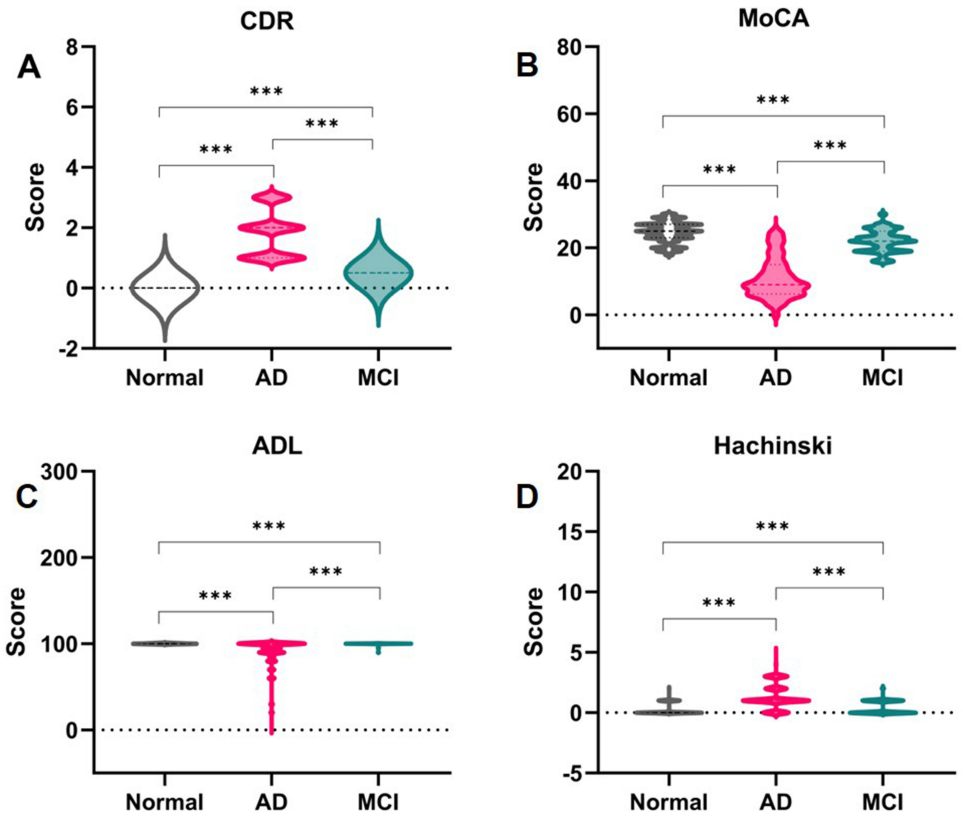

Figure 4 Comparison of scores among normal population, AD population, and MCI population. (**A**) CDR score. (**B**) MoCA score. (**C**) ADL score. (**D**) Hachinski score. ***: $p<0.001$.

provide beneficial support for memory health and physical health in at-risk populations for AD.[13,14] This study suggests that effective prevention and control of AD should focus on low-education manual laborers, with particular attention given to women. Early intervention in the form of cognitive and memory training for these populations may help reduce the incidence of AD and MCI. During the course of this study, we provided educational guidance on memory training via digital applications and video games to suitable populations. We hope to further explore the effects of these methods on maintaining memory ability in cognitively declining populations in southwestern China during follow-up observations.

In addition to the common factors influencing AD onset, such as advanced age, a family history of dementia, alcohol abuse, and comorbidities across various systems, these factors significantly impact the development of AD or MCI.[15–17] This study demonstrated that MCI, as a precursor symptom related to AD, progressively increases after the age of 60 years. In the survey area, the occurrence of AD becomes more pronounced after the age of 80 years than before 80 years, indicating that cognitive decline becomes more common as individuals become older. For the local elderly population, the period after 80 years of age represents an acceleration phase for cognitive decline, particularly for AD, which also complicates symptom management.[18,19] This finding underscores the necessity of early screening for MCI and emphasizes the importance of maintaining window periods for systematic treatment of AD before the age of 80. This study revealed that the most prominent comorbidity in AD patients was neurological disorders. Dizziness, migraine, and epilepsy were identified as the most common central nervous system comorbidities, with some studies already exploring the association between epilepsy and AD onset,[20] suggesting that epilepsy as a neurological comorbidity may be a high-risk factor for AD. Additionally, this study revealed that among circulatory system comorbidities, hypertension was the most common, followed by coronary heart disease. A meta-analysis explored the relationship between hypertension and the occurrence of neurofibrillary tangles and amyloid plaques in AD autopsy samples,[21] indicating that early, standardized treatment of hypertension may play a role in the prevention and control of AD.[22] Respiratory diseases such as

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asthma[23] and chronic obstructive pulmonary disease (COPD),[24] as well as endocrine disorders such as thyroid dysfunction[25] and diabetes,[26] may also influence the onset and progression of AD. Emotional factors and sleep disturbances have long been focal points in the study of psychiatric disorders, and this study similarly confirmed their impact on AD risk. Future research could explore the causal relationships between systemic diseases and AD initiation.

In addition to the common characteristics shared with other studies, this research also revealed several unique risk factors. The southwestern region of China, which is a major tobacco-producing area, has a high prevalence of smoking among local elderly individuals. This study revealed that smoking increased the risk of developing MCI but was not a risk factor for AD. This finding is inconsistent with the conventional belief that smoking is a risk factor for AD.[27] There is ongoing debate about the effects of nicotine and other chemicals in tobacco on memory function.[28–30] On the basis of our results, smoking-related chronic obstructive pulmonary disease, hypertension, and cerebrovascular diseases may contribute to cognitive decline, but the direct pathogenic relationship with AD requires further investigation. This study also included surgical history in the risk analysis, revealing that both a history of surgeries and the number of surgeries could be risk factors for AD. Previous studies have suggested that cranial surgeries might be risk factors for AD,[31] and there is no strong support for the hypothesis that exposure to general anaesthesia significantly increases AD incidence.[32] Therefore, the correlation between surgical history and the incidence of AD among residents in southwestern China is a noteworthy issue that merits further exploration. Additionally, the southwestern region is known for its high calcium content in water, making it a high-prevalence area for urolithiasis. In this study, urological comorbidities, primarily urolithiasis, were identified as risk factors for AD, which is consistent with previous reports.[33] Whether this is a coincidental finding remains to be studied further.

The identification of surgical history and urinary calculi as region-specific risk factors for AD in Southwest China points to plausible biological and environmental mechanisms that warrant further investigation. In the case of surgical procedures, perioperative systemic inflammation may serve as a key mediator: surgical trauma triggers the release of pro-inflammatory cytokines (eg, TNF-α, IL-6), which can cross the blood-brain barrier and promote amyloid-β deposition and tau hyperphosphorylation-core pathological features of AD.[34,35] Furthermore, certain anesthetics (eg, volatile agents) may disrupt neuronal cholinergic signaling or induce neuroinflammation, thereby contributing to long-term cognitive decline, particularly in vulnerable individuals with pre-existing vascular or genetic risks.[36] Postoperative cognitive dysfunction (POCD), a common complication of major surgery, may also represent a prodromal stage or accelerate progression to overt AD.[37]

Regarding urinary calculi, chronic inflammation and systemic metabolic disturbances represent potential linking pathways. Recurrent urinary stones are often associated with chronic urinary tract infections (UTIs) and localized inflammation, which can propagate a state of low-grade systemic inflammation a recognized risk factor for AD pathogenesis.[38] Moreover, dietary habits (eg, high calcium/oxalate intake) and regional environmental factors (eg, hard water common in Southwest China) that predispose individuals to urinary calculi may also influence cerebral metabolism. For instance, excessive calcium accumulation can disrupt neuronal calcium homeostasis, while oxalate-induced oxidative stress may damage hippocampal neurons essential for memory formation.[39,40]

Together, these mechanisms suggest that surgical history and urinary calculi may act as physiological or environmental "stressors" that exacerbate AD pathogenesis through inflammatory, metabolic, and dietary pathways particularly in regions with distinct socioeconomic and healthcare profiles. Further mechanistic studies, such as longitudinal monitoring of inflammatory markers after surgery or metabolic profiling of calculi patients, are needed to validate these pathways and guide targeted preventive strategies.

This study, together with previous evidence, indicates that cigarette smoking exerts a significantly differential impact onMCI and AD: smoking is an established risk factor for MCI, increasing its incidence in a dose-dependent manner, whereas its direct association with AD is weak or non-significant, which contradicts the traditional view that smoking is a risk factor for AD.[41]

The underlying mechanisms are linked to disease stage specificity and the dual effects of nicotine. During the MCI stage, smoking impairs the function of key cognitive brain regions such as the hippocampus by inducing oxidative stress, activating neuroinflammation (with the release of IL-6 and TNF-α), and damaging cerebral microvessels.[42,43] In contrast, during the AD stage, extensive neurodegeneration and core pathological changes including Aβ deposition and tau

Table 3 Multivariate Logistic Regression Analysis of the AD Group and MCI Group

	Normal Cognitive (n=9680)	AD (n=722)	Miltivariable OR (95% CI)	*p* value	MCI (n= 1920)	Multivariable OR (95% CI)	*p* value
Prevalence		5.81%			15.46%		
Sex							
Male	4917(50.80)	294(40.72)	1.00		847(44.11)	1.00	
Female	4763(49.20)	428(59.28)	1.32(1.03–1.68)	0.026	1073(55.89)	0.87(0.75–1.00)	0.056
Age group (year)							
60-69	2456(25.37)	157(21.75)	1.00		120(6.25)	1.00	
70-79	5997(61.95)	336(46.54)	0.83(0.65–1.06)	0.128	1512(78.75)	5.32(4.27–6.63)	<0.001
>80	1227(12.68)	229(31.72)	2.51(1.88–3.35)	<0.001	288(15.00)	4.53(3.48–5.90)	<0.001
Ethnic groups							
Han nationality	8907(92.01)	625(86.57)	1.00		1623(84.53)	1.00	
Ethnic minorities	773(7.99)	97(13.43)	1.22(0.87–1.70)	0.245	297(15.47)	2.16(1.79–2.62)	<0.001
Parental history of dementia							
No	7215(74.54)	410(56.79)	1.00		997(51.93)	1.00	
Yes	289(2.99)	88(12.19)	3.60(2.41–5.38)	<0.001	175(9.11)	4.93(3.60–6.74)	<0.001
Unknown	2176(22.48)	224(31.02)	1.60(1.24–2.06)	<0.001	748(38.96)	5.05(4.17–6.13)	<0.001
Residence location							
Urban	5118(52.87)	257(35.60)	1.00		891(46.41)	1.00	
Rural	4562(47.13)	465(64.40)	2.17(1.75–2.68)	<0.001	1029(53.59)	1.13(0.99–1.28)	0.067
Education level, year							
<1	2288(23.64)	208(28.81)	1.00		899(46.82)	1.00	
1-3	996(10.29)	124(17.17)	1.50(1.09–2.06)	0.013	148(7.71)	0.37(0.29–0.47)	<0.001
4-6	1720(17.77)	121(16.76)	0.69(0.50–0.95)	0.022	101(5.26)	0.13(0.10–0.17)	<0.001
>6	4676(48.31)	269(37.26)	0.53(0.41–0.69)	<0.001	772(40.21)	0.36(0.31–0.42)	<0.001
Live together							
Live alone	309(3.19)	18(2.49)	–		353(18.39)	1.00	
Husband and wife	7074(73.08)	355(49.17)	–	–	1117(58.18)	0.25(0.20–0.32)	<0.001
Children and children	1973(20.38)	172(23.82)	–	–	297(15.47)	0.08(0.06–0.10)	<0.001
Other	324(3.35)	177(24.52)	–	–	153(7.97)	0.30(0.21–0.43)	<0.001
Occupation							
Manual labor	6001(61.99)	569(78.81)	1.00		992(51.67)	1.00	
Mental work	1602(16.55)	69(9.56)	0.53(0.38–0.75)	<0.001	336(17.50)	2.06(1.71–2.49)	<0.001
Unemployed/other	2077(21.46)	84(11.63)	0.27(0.20–0.37)	<0.001	592(30.83)	1.59(1.37–1.84)	<0.001
Current smoker							
No	7571(78.21)	559(77.42)	–		1531(79.74)	–	
Yes	2109(21.79)	163(22.58)	–	–	389(20.26)	–	–
Current drinking							
No	9196(95.00)	664(92.22)	1.00		1847(96.20)	1.00	
Yes	484(5.00)	56(7.78)	2.41(1.57–3.69)	<0.001	73(3.80)	0.88(0.64–1.21)	0.42
Nervous system diseases							
No	9535(98.50)	490(67.87)	1.00		1824(95.00)	1.00	
Yes	145(1.50)	232(32.13)	12.38(7.24–21.17)	<0.001	96(5.00)	1.90(1.04–3.49)	0.038
Cerebrovascular disease							
No	9591(99.08)	514(71.19)	1.00		1859(96.82)	1.00	
Yes	89(0.92)	208(28.81)	3.36(1.83–6.18)	<0.001	61(3.18)	1.89(0.90–3.98)	0.093
Cardiovascular diseases							
No	5988(61.86)	306(42.38)	1.00		1048(54.58)	1.00	
Yes	3692(38.14)	416(57.62)	2.16(1.76–2.64)	<0.001	872(45.42)	1.39(1.23–1.58)	<0.001
Respiratory diseases							
No	9426(97.38)	611(84.63)	1.00		1483(77.24)	1.00	
Yes	254(2.62)	111(15.37)	6.79(4.83–9.53)	<0.001	437(22.76)	11.71(9.48–14.47)	<0.001
Endocrine system diseases							
No	8297(85.71)	511(70.78)	1.00		1567(81.61)	1.00	
Yes	1383(14.29)	211(29.22)	2.17(1.71–2.75)	<0.001	353(18.39)	1.15(0.97–1.37)	0.109

(*Continued*)

Table 3 (Continued).

	Normal Cognitive (n=9680)	AD (n=722)	Miltivariable OR (95% CI)	*p* value	MCI (n= 1920)	Multivariable OR (95% CI)	*p* value
Urinary system diseases							
No	9358(96.67)	552(76.45)	1.00		1752(91.25)	1.00	
Yes	322(3.33)	170(23.55)	9.57(7.18–12.75)	<0.001	168(8.75)	2.81(2.12–3.72)	<0.001
Digestive system diseases							
No	8249(85.22)	620(85.87)	–		1740(90.63)	1.00	
Yes	1431(14.78)	102(14.13)	–	–	180(9.38)	0.32(0.25–0.41)	<0.001
Emotion							
Stability	9318(96.26)	651(90.17)	1.00		1552(80.83)	1.00	
Indifferent	258(2.67)	44(6.09)	1.99(1.25–3.16)	0.004	270(14.06)	6.67(5.25–8.48)	<0.001
Irritable	104(1.07)	27(3.74)	3.96(2.17–7.22)	<0.001	98(5.10)	5.78(4.00–8.34)	<0.001
Surgical history							
None	7012(72.44)	276(38.23)	1.00		1216(63.33)	1.00	
1	2485(25.67)	284(39.34)	2.88(2.32–3.58)	<0.001	646(33.65)	1.56(1.37–1.79)	<0.001
>1	183(1.89)	162(22.44)	18.80(13.41–26.36)	<0.001	58(3.02)	1.63(1.09–2.44)	0.018
Sleep awakening time							
>3 h	1610(16.63)	114(15.79)	–		157(8.18)	–	
1-3 h	5002(51.67)	408(56.51)	–	–	1518(79.06)	–	–
<1 h	3068(31.69)	200(27.70)	–	–	245(12.76)	–	–
Sleep duration							
<4 h	77(0.80)	93(12.88)	1.00		83(4.32)	1.00	
4-8 h	5282(54.57)	366(50.69)	0.06(0.04–0.10)	<0.001	1268(66.04)	0.04(0.02–0.07)	<0.001
>8 h	4321(44.64)	263(36.43)	0.05(0.03–0.09)	<0.001	569(29.64)	0.03(0.02–0.04)	<0.001

Note: Data are n (%) or mean (SD) unless specified otherwise.

phosphorylation have already formed, masking the additional effects of smoking.[44] Nicotine exhibits both neuroprotective and neurotoxic effects: low-dose nicotine can upregulate nicotinic acetylcholine receptors (nAChRs) and promote Aβ clearance, while high-dose nicotine leads to receptor desensitization and exacerbated oxidative stress.[45,46]

In clinical practice, smoking cessation exerts significant cognitive protective effects on individuals at high risk of MCI, whereas AD patients mainly benefit from improved overall health after quitting smoking. Future prospective studies are needed to clarify the dynamic role of nicotine in MCI-to-AD conversion, thereby providing evidence for precision intervention strategies.

Study Limitations

While this study provides valuable insights into the epidemiology of AD and MCI in southwestern China, several limitations should be considered. First, although a large sample was achieved, the sampling method, which relied on voluntary participation from communities, may introduce potential selection bias. Individuals with severe cognitive impairment or those with limited mobility might have been underrepresented, potentially leading to an underestimation of the true prevalence. Second, diagnostic variability, despite the use of standardized tools (eg, CDR, MoCA), remains a concern as clinical diagnoses can be influenced by the assessors' expertise and the subjective reporting of symptoms by patients and caregivers, particularly for MCI classification. Furthermore, the cross-sectional nature of this study limits the ability to establish causal inferences from the identified risk factors. Residual confounding from unmeasured or imprecisely measured variables, such as detailed socioeconomic status across the lifespan or specific genetic factors, may also influence the results.

Placing our findings within an international context provides a broader perspective. The AD prevalence of 5.81% in our cohort is higher than the global average of approximately 3.9% for individuals aged 60+ and the reported prevalence in many developed countries.[7] This elevated rate shares similarities with trends observed in

other developing regions with historical educational and resource limitations, suggesting shared socioeconomic determinants of brain health. The stark urban-rural disparity and the strong association with manual labor and low education observed in our study echo findings from other rapidly developing nations, highlighting a global pattern where cognitive health inequities are linked to developmental disparities. Conversely, the relationship between certain modifiable risk factors, such as hypertension and sleep disorders, with AD and MCI is consistent with reports from Western cohorts,[21,22] reinforcing the universal importance of managing vascular and lifestyle factors for cognitive preservation. The unique regional findings, such as the role of urolithiasis and surgical history as potential risk factors, warrant further investigation in other populations to determine their generalizability.

Conclusion

In conclusion, the prevalence of cognitive impairment among elderly individuals in southwestern China is relatively high, and the risk factors associated with AD are complex. Common issues such as advanced age, a family history of dementia, alcohol abuse, and comorbidities across various systems play a role in the pathogenesis of AD. Notably, factors such as smoking history, surgical history, and urological comorbidities have certain regional characteristics associated with AD onset. These findings suggest that the development of AD is influenced by various factors, including region, environment, and ethnicity. Therefore, AD prevention and treatment efforts should be tailored to the specific characteristics of different regions.

Based on our findings, we recommend that future public health strategies prioritize the following areas: developing integrated intervention models combining digital cognitive training and vascular risk management for high-risk groups, particularly older rural women with limited education; incorporating brief cognitive screening into routine primary care chronic disease management to enable early detection and intervention; and establishing prospective follow-up cohorts to clarify the causal relationships between region-specific risk factors (such as urolithiasis and surgical history) and cognitive decline, thereby informing tailored regional prevention strategies.

Data Sharing Statement

The research data can be disclosed at the corresponding author, and those who need research can contact the corresponding author XQR.

Ethics Approval

This study was approved by the ethics committee of the Affiliated Hospital of Zunyi Medical University. The study followed the Declaration of Helsinki.

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Author Contributions

Co-first authors: Yuhang Zhu and Hongli Liu. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas;

took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest.

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