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Correlation between serum lipid profiles and cognitive impairment in old age: a cross-sectional study

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ABSTRACT

Background The correlation between cognitive function and lipid profiles, including total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglycerides, is inconsistent.

Aims This cross-sectional study investigated the association between serum lipid levels and the prevalence of cognitive impairment among community-dwelling older adults and explored this difference in association by gender and urban-rural residency.

Methods Participants aged 65 and above in urban and rural areas were recruited between 2018 and 2020, selected from the Hubei Memory and Aging Cohort Study. Detailed neuropsychological evaluations, clinical examinations and laboratory tests were conducted in community health service centres. Multivariate logistic regression was used to analyse the correlation between serum lipid profiles and the prevalence of cognitive impairment.

Results We identified 1 336 cognitively impaired adults (≥65 years)—1 066 with mild cognitive impairment and 270 with dementia—from 4 746 participants. Triglycerides level was correlated with cognitive impairment in the total sample (χ^2=6.420, p=0.011). In gender-stratified multivariate analysis, high triglycerides in males reduced the risk of cognitive impairment (OR: 0.785, 95% CI: 0.623 to 0.989, p=0.040), and high LDL-C in females increased the risk of cognitive impairment (OR: 1.282, 95% CI: 1.040 to 1.581, p=0.020). In both gender-stratified and urban-rural stratified multivariate analyses, high triglycerides reduced the risk of cognitive impairment in older urban men (OR: 0.734, 95% CI: 0.551 to 0.977, p=0.034), and high LDL-C increased the risk of cognitive impairment in older rural women (OR: 1.830, 95% CI: 1.119 to 2.991, p=0.016).

Conclusions There are gender and urban-rural differences in the correlation of serum lipids with cognitive impairment. High triglycerides levels may be a protective factor for cognitive function in older urban men, while high LDL-C levels may be a risk factor for cognitive function in older rural women.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The correlation between lipid profiles and cognitive function remains controversial. Most epidemiological studies were performed in high-income countries with generally well-educated participants. Less is known about the correlation in rural areas of less developed areas like Central China.

WHAT THIS STUDY ADDS

⇒ This study found that the correlation between blood lipids and cognitive impairment differed by gender and urban-rural regions.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Different strategies should be developed for men and women when it comes to preventing cognitive impairment. Rural-dwelling older adults should be considered a priority for the prevention of cognitive impairment.

INTRODUCTION

Cognitive impairment includes mild cognitive impairment (MCI) and dementia and is increasing rapidly with the ageing of the population. In 2018, China had 15.07 million patients with dementia, including 9.83 million with Alzheimer's disease and 38.77 million patients with MCI.[1] This has brought a huge health burden to Chinese society and has become one of the major health issues in the country.[2] Existing studies suggest that dyslipidaemia is associated with cognitive impairment.[3 4] The level of serum lipids gradually increases as individuals age and their lifestyles undergo changes; thus, with the increasing number of older persons, the prevalence of dyslipidaemia has increased significantly.[5] A national survey in China showed that the prevalence of hypercholesterolaemia and hypertriglyceridaemia among adults was 6.9% and 13.8%, respectively.[6] Therefore, it is crucial to understand the correlation between serum lipid levels and cognitive performance in the Chinese population, especially among elders.

Dyslipidaemia, as a modifiable risk factor, is one of the most important factors leading to atherosclerosis. It is also an independent risk factor for coronary heart disease and ischaemic stroke,[7] which increase the risk of cognitive impairment in older adults.[8] However, conflicting results have been found regarding the correlation of cognitive impairment with serum total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglycerides levels.[9 10] A case–control study showed that cognitive performance test results changed with levels of serum TC and LDL-C concentrations in older adults.[11] Another study showed that high LDL-C is a risk factor for cognitive impairment in older women.[12] To the contrary, a meta-analysis did not find a significant relationship between TC, HDL-C or LDL and the risk of cognitive decline in older adults averaging 76 years of age.[13] We speculate that the inconsistency is related to gender and urban-rural differences. However, only a few studies with relatively small samples have analysed the relationship between serum lipids and cognitive impairment while looking at differences in gender and urban-rural regional disparities. There are no reports on the correlation between cognitive function and lipid profiles in older individuals from rural areas in Central China; most reports are from relatively developed regions of the country. Therefore, further studies are necessary to clarify the correlation between cognitive impairment and lipid profiles by gender and urban-rural regional differences in Central China. Based on a cross-sectional investigation of the Hubei Memory and Aging Cohort Study (HMACS), this study explored the relationship between serum lipids and cognitive impairment in community-dwelling older adults in China and evaluated the gender and urban-rural differences.

METHODS

Study participants

The HMACS was designed as a community-based cohort study with urban and rural settings, which was carried out between 2018 and 2020; it was designed to assess the prevalence and incidence of cognitive impairment, particularly Alzheimer's disease, and the prevalence of related risk factors in older adults.[14] In this study, cluster random sampling method was used to select four community health service centers in Wuhan and 48 villages in Dawu County. This study included participants who met the following eligibility criteria: (1) aged 65 and older; (2) with electronic medical records kept in community health centres or hospitals; (3) with completed cognitive evaluation data; and (4) with blood TC, LDL-C, HDL-C and triglyceride information. Potential participants were excluded if they (1) were not traceable; (2) showed mental retardation or dementia on their medical record; (3) had severe hearing and vision impairment and were not able to participate actively in the neuropsychological assessments. Written informed consent or witnessed oral consent was obtained from all participants after the nature of the procedures had been fully explained. Among 8 221 older residents, 2 109 were excluded due to illness or other reasons and 1 366 were unable to complete the survey. Of the enrollees, 4 746 eligible participants completed the full-length survey (figure 1).

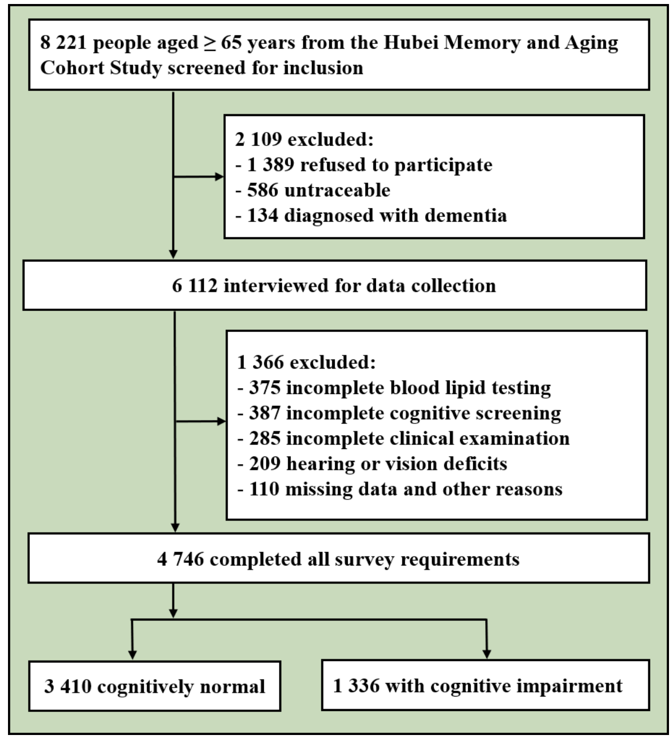

Figure 1 Flowchart of the study.

Neuropsychological assessment

The overall cognitive function and subdomains of the older adults were assessed with a structured neuropsychological scale. Tools used for assessment included the Mini-Mental State Examination (MMSE)[15] and the Chinese version of the Montreal Cognitive Assessment-Basic (MOCA-BC)[16] to assess global cognition, the Auditory Verbal Learning Test[17] to assess memory, the Trail-Making Tests A (TMT-A) and B (TMT-B) to assess executive function, the forward and backward of the Digit Span Test to assess attention, the Boston Naming Test[18] and the Animal Fluency Test to assess language, and the Clock-Drawing Test to assess visuospatial ability.[19]

The Activities of Daily Living Scale (ADL)[20] was used to assess participants' day-to-day life skills and activities, and the Geriatric Depression Scale 15[21] was used to assess depression in the past week.

Diagnosis of cognitive impairment

Cognitive impairment here refers to MCI and dementia. After each participant was examined, a panel of two neuroscientists and two neuropsychologists with expertise in dementia diagnosed dementia and MCI. HMACS reached a diagnostic consensus for dementia using the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria[22]: (1) previous normal cognition, (2) cognitive decline or abnormal mental behaviour, (3) decline affects work ability or daily life and (4) cannot be explained by delirium or other mental illness. For MCI, Petersen's criteria were used[23]: (1) concern of a cognitive change by the participant, informant or clinician based on information obtained during the clinical interview; patients, insiders and/or clinicians report or find cognitive impairment; (2) objective impairment on any neuropsychological test within a cognitive domain (mainly based on MMSE and MOCA-BC scores); (3) essentially normal functional activities (as assessed by ADL); and (4) absence of dementia.

Serum lipid test

Participants were asked to abstain from alcohol and high-fat foods 24 hours before blood collection. After fasting for 10–12 hours, 3 mL of fasting venous blood was extracted in the early morning, and the levels of TC, triglycerides, LDL-C and HDL-C were detected by an automatic biochemical analyser. According to the 2016 Chinese Adult Dyslipidemia Prevention Guideline, normal blood lipids were defined as TC <5.2 mmol/L, triglycerides <1.7 mmol/L, LDL-C <3.4 mmol/L and HDL-C >1.0 mmol/L. For participants taking lipid-lowering drugs, they were defined as having normal lipid levels if their lipid levels were within the normal range.

Other covariants

Other covariants included demographic characteristics (age, sex, education level, marital status and residence), lifestyle (smoking, drinking, physical exercise and intellectual activity) and disease history (hypertension and diabetes), which were collected using a dedicated form. Physical and clinical examinations (height, weight, blood pressure, head circumference, waist circumference and hip circumference) were performed by nurses.

Sex was divided into male and female. Age was divided into four groups: 65–69, 70–74, 75–79 and 80 years old and above. The level of education included three categories: primary school or below, middle school, and university or above. Marital status was divided into two groups: married and unmarried. Residence was divided into rural and urban areas. Current smoking referred to smoking ≥1 cigarette/day within the last 6 months, consistent with the definition of the 2010 National Smoking Survey of Chinese Adults.[24] Drinking was defined as consuming >14 drinks/week for men (seven drinks/week for women) for ≥1 year, and one drink was defined as 14 g of pure alcohol, which equates to a 150 mL glass of wine, a 350 mL can of beer or two shots of spirits.[25] Physical activities were estimated by recalling the frequency and time spent on nine activities, such as walking, dancing, jogging or playing sports in a typical week, according to the guidelines for Chinese adults.[26] Intellectual activities were defined as activities like reading, writing, playing chess/poker/mahjong or using an app for playing games ≥3 times/week for ≥30 min/activity.[27] Hypertension was self-reported as a diagnosis and/or use of antihypertensive medication within 2 weeks prior to the study.[28] Diabetes was self-reported as a diagnosis previously determined by a healthcare professional or current use of antidiabetic medications.[29]

Statistical analyses

SPSS V.26.0 was used for all statistical analyses (SPSS). Continuous variables were denoted as mean (standard deviation (SD)) or median (interquartile range (IQR)). Categorical variables were expressed as numbers (percentages). Differences between study groups were assessed using Student's t-tests for continuous variables with normal distribution, rank tests for continuous variables with skewed distribution and χ^2 tests for categorical variables.

Univariate logistic regression was used to analyse the relationship between lipid levels and the rate of cognitive impairment, and the above-mentioned various factors were included in the multivariate logistic regression analysis. Based on single-factor analysis, we used multiple logistic regression analysis in all study participants to adjust for confounding factors and to further explain the effects of serum lipids on cognitive impairment.

We also performed stratified analysis. The total population was divided into two gender subgroups and two residence subgroups according to gender and urban-rural regions. Then, these groups were further divided into four subgroups according to both genders and urban-rural regions. A stratified logistic regression model was used to evaluate the relationship between serum lipids and cognitive impairment among different genders and regions. All p values were bilateral, and results were considered to be statistically significant when p<0.05.

RESULTS

Characteristics of study participants

As shown in table 1, a total of 4 746 community adults aged ≥65 were included in this study, with a mean (SD) age of 71.6 (5.5), including 2 166 males (45.6%) and 2 580 females (54.4%). 80.7% of the participants were married; 1 323 (27.9%) were from remote rural areas, 3 423 (72.1%) were from urban areas; 927 (19.5%) had a college education or above; 3 972 (83.7%) and 2 980 (62.8%) regularly participated in physical exercise and intellectual activities; 3 134 (66.0%) of them had hypertension, 807 (17.0%) had diabetes, 708 (14.9%) had coronary heart disease and 882 (18.6%) had cerebrovascular disease; 1 767 (37.2%) had abnormal TC levels, 1 477 (31.1%) had abnormal triglyceride levels, 1 094 (23.1%) had abnormal LDL-C levels and 821 (17.3%) had abnormal HDL-C levels.

Older adults with cognitive impairment accounted for 35.8% of the rural-dwelling and 25.2% of the urban-dwelling participants, respectively. The cognitive impairment group was less educated, had more unmarried participants, was less likely to engage in physical exercise and intellectual activities and had a higher prevalence of high blood pressure, diabetes, coronary heart disease and cerebrovascular disease. There were significant differences in age, education, marital status, physical exercise habits, intellectual activity habits, eating animal fat, hypertension, diabetes and cerebrovascular disease between the normal cognition and the cognitive impairment groups (p<0.05) for the total and urban-dwelling

Table 1 General characteristics of participants

Characteristics	Total (%) Normal cognition (n=3 410)	Total (%) Cognitive impairment (n=1 336)	Rural (%) Normal cognition (n=849)	Rural (%) Cognitive impairment (n=474)	Urban (%) Normal cognition (n=2 561)	Urban (%) Cognitive impairment (n=862)
Gender	p=0.179		p=0.702		p=0.176	
Male	1 577 (46.2)	589 (44.1)	389 (45.8)	212 (44.7)	1 188 (46.4)	377 (43.7)
Age (years)	p<0.001***		p<0.001***		p<0.001***	
65–69	1 672 (49.0)	409 (30.6)	343 (40.4)	133 (28.1)	1 329 (51.9)	276 (32.0)
70–74	1 038 (30.4)	413 (30.9)	287 (33.8)	166 (35.0)	751 (29.3)	247 (28.7)
75–79	441 (12.9)	255 (19.1)	137 (16.1)	99 (20.9)	304 (11.9)	156 (18.1)
≥80	259 (7.6)	259 (19.4)	82 (9.7)	76 (16.0)	177 (6.9)	183 (21.2)
Marital status	p<0.001***		p=0.053		p<0.001***	
Married	2 851 (83.6)	978 (73.2)	559 (65.8)	310 (65.4)	2 252 (87.9)	668 (77.5)
Education level	p<0.001***		p=0.235		p<0.001***	
Primary school or below	941 (27.6)	553 (41.4)	687 (80.9)	365 (77.0)	254 (9.9)	188 (21.8)
Middle school	1 767 (51.8)	558 (41.8)	149 (17.6)	101 (21.3)	1 618 (63.2)	457 (53.0)
University or above	702 (20.6)	225 (16.8)	13 (1.5)	8 (1.7)	689 (26.9)	217 (25.2)
Smoking history	p=0.053		p=0.384		p=0.003**	
Yes	990 (29.0)	356 (26.6)	258 (30.4)	155 (32.7)	732 (28.6)	201 (23.3)
Drinking history	p=0.112		p=0.908		p=0.009**	
Yes	793 (23.3)	282 (21.1)	225 (26.5)	127 (26.8)	568 (22.2)	155 (18.0)
Physical exercise	p<0.001***		p=0.111		p<0.001***	
Yes	2 913 (85.4)	1 059 (79.3)	631 (74.3)	333 (70.3)	2 282 (89.1)	726 (84.2)
Cognitive activity	p<0.001***		p=0.345		p<0.001***	
Yes	2 263 (66.4)	717 (53.7)	334 (39.3)	174 (36.7)	1 929 (75.3)	543 (63.0)
Eating animal fat	p<0.001***		p=0.828		p<0.001***	
Yes	1 558 (45.7)	498 (37.3)	279 (32.9)	153 (32.3)	1 279 (49.9)	345 (40.0)
Hypertension	p=0.002**		p=0.426		p=0.006**	
Yes	2 207 (64.7)	927 (69.4)	584 (68.8)	336 (70.9)	1 623 (63.4)	591 (68.6)
Diabetes	p=0.008**		p=0.339		p<0.001***	
Yes	549 (16.1)	258 (19.3)	101 (11.9)	63 (13.3)	448 (17.5)	193 (22.4)
TC	p=0.719		p=0.567		p=0.324	
High TC	1 265 (37.1)	502 (37.6)	309 (36.3)	164 (34.5)	956 (37.3)	338 (39.2)
TG	p=0.011*		p=0.313		p=0.075	
High TG	1 098 (32.2)	379 (28.4)	227 (26.7)	114 (24.1)	871 (34.0)	265 (30.7)
LDL-C	p=0.746		p=0.540		p=0.578	
High LDL-C	798 (23.4)	296 (22.2)	104 (12.2)	54 (11.4)	694 (27.1)	242 (28.1)
HDL-C	p=0.186		p=0.564		p=0.994	
Low HDL-C	617 (18.1)	204 (15.3)	74 (8.7)	39 (8.2)	282 (11.0)	95 (11.0)

*p<0.05; **p<0.01; ***p<0.001.
HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride.

participants, but not for rural-dwelling participants. For more details, please see the online supplemental file.

Prevalence of cognitive impairment by dyslipidaemia rate in the gender and urban-rural residence groupings

Figure 2 shows the prevalence of cognitive impairment by gender and urban-rural groups. There was no significant difference in the prevalence of cognitive impairment between the normal TC group and the high TC group in the total population. After gender and urban-rural stratification analyses, the prevalence of cognitive impairment between the normal TC group and the high TC group was also not significantly different (figure 2A). In the total population, the prevalence of cognitive impairment was lower in the high triglycerides group than in the normal triglycerides group (χ^2=6.420, p=0.011), and the same result was observed in the

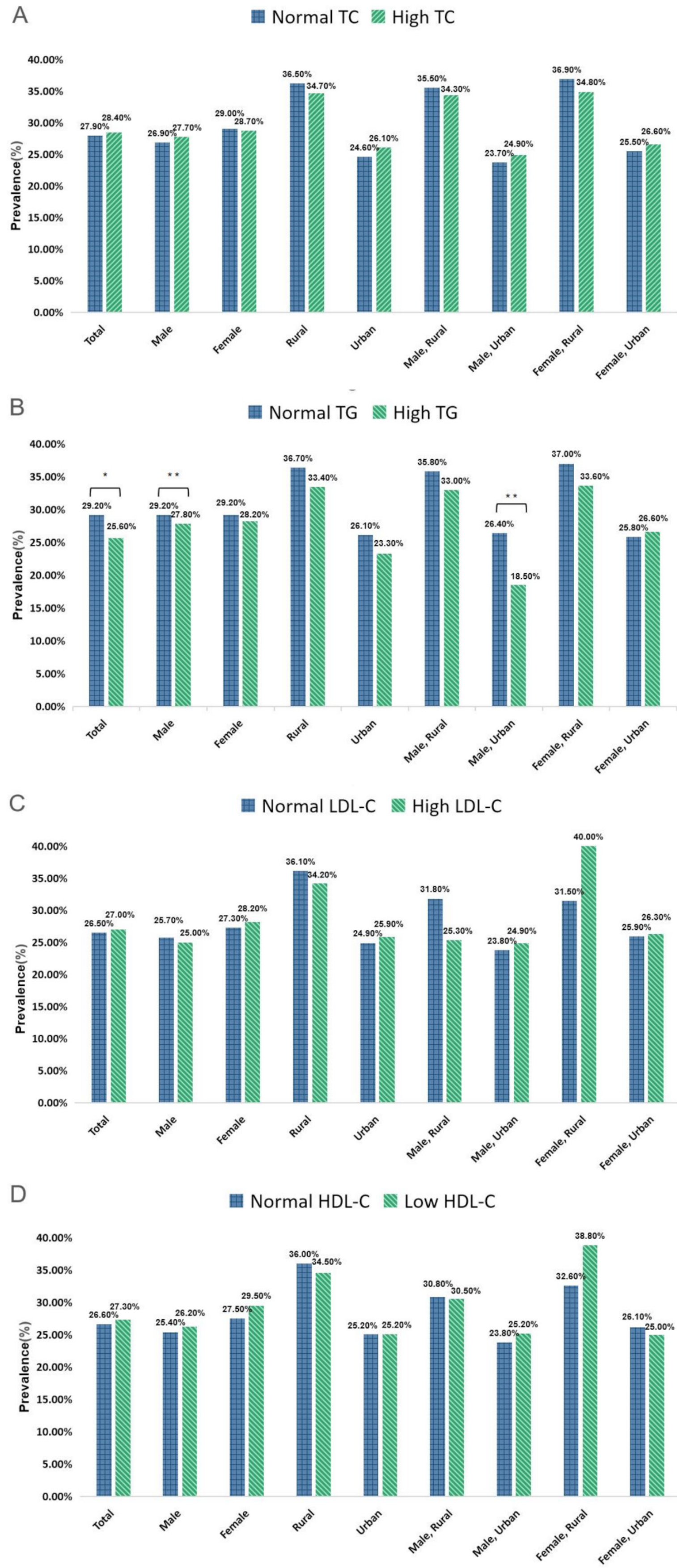

Figure 2 Prevalence of cognitive impairment by dyslipidaemia rate in the gender and urban-rural residence groupings. (A) Total cholesterol (TC). (B) Triglyceride (TG). (C) Low-density lipoprotein cholesterol (LDL-C). (D) High-density lipoprotein cholesterol (HDL-C). *p<0.05; **p<0.01.

male and urban male subgroups (χ^2=11.837, p=0.001; χ^2=11.190, p=0.001) (figure 2B). In the total population, there was no significant difference in the prevalence of cognitive impairment between the normal LDL-C group and the high LDL-C group. After being stratified by gender and urban-rural regions, the prevalence of cognitive impairment was not significantly different (figure 2C). This also held for the normal HDL-C group and low HDL-C group (figure 2D).

Relationships between serum lipids and cognitive impairment with multivariate analysis

In order to explore the relationship between serum lipids and cognitive impairment, we conducted multivariate stratified analysis (table 2). In model 1, no potential confounding variables were added. After stratified analysis, we found that high triglycerides levels were associated with a lower risk of cognitive impairment in the total population (OR: 0.836, 95% CI: 0.727 to 0.960, p=0.011),

Table 2 Relationships between serum lipid and cognitive impairment by multivariate analysis

	Total		Rural		Urban	
Variable	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**
Model 1						
Total						
High TC	1.024 (0.899 to 1.167)	0.719	0.934 (0.738 to 1.182)	0.567	1.083 (0.924 to 1.269)	0.324
High TG	0.836 (0.727 to 0.960)	0.011*	0.875 (0.674 to 1.134)	0.313	0.860 (0.728 to 1.015)	0.075
High LDL-C	1.026 (0.879 to 1.197)	0.746	1.119 (0.780 to 1.607)	0.540	1.050 (0.884 to 1.247)	0.578
Low HDL-C	1.038 (0.841 to 1.282)	0.726	1.130 (0.746 to 1.710)	0.564	1.001 (0.782 to 1.281)	0.994
Male						
High TC	1.039 (0.840 to 1.285)	0.727	0.948 (0.654 to 1.375)	0.779	1.064 (0.819 to 1.383)	0.640
High TG	0.679 (0.544 to 0.847)	0.001**	0.884 (0.592 to 1.321)	0.548	0.633 (0.483 to 0.823)	0.001**
High LDL-C	0.963 (0.747 to 1.242)	0.771	0.729 (0.397 to 1.339)	0.309	1.059 (0.799 to 1.404)	0.690
Low HDL-C	1.045 (0.795 to 1.374)	0.751	0.984 (0.542 to 1.786)	0.958	1.081 (0.794 to 1.472)	0.622
Female						
High TC	0.987 (0.832 to 1.171)	0.880	0.912 (0.670 to 1.243)	0.561	1.057 (0.859 to 1.301)	0.598
High TG	0.954 (0.796 to 1.142)	0.606	0.863 (0.613 to 1.216)	0.401	1.042 (0.840 to 1.292)	0.709
High LDL-C	1.042 (0.856 to 1.269)	0.678	1.445 (0.913 to 2.289)	0.116	1.020 (0.818 to 1.271)	0.861
Low HDL-C	1.028 (0.729 to 1.449)	0.875	1.315 (0.736 to 2.352)	0.335	0.940 (0.613 to 1.440)	0.776
Model 2						
Total						
High TC	1.096 (0.956 to 1.256)	0.194	1.013 (0.795 to 1.291)	0.914	1.136 (0.961 to 1.343)	0.136
High TG	0.940 (0.813 to 1.088)	0.409	0.929 (0.711 to 1.215)	0.591	0.959 (0.804 to 1.143)	0.641
High LDL-C	1.159 (0.986 to 1.362)	0.073	1.225 (0.845 to 1.776)	0.285	1.127 (0.940 to 1.351)	0.198
Low HDL-C	0.966 (0.774 to 1.204)	0.759	1.081 (0.706 to 1.657)	0.719	0.939 (0.724 to 1.218)	0.635
Male						
High TC	1.073 (0.859 to 1.340)	0.536	0.986 (0.670 to 1.452)	0.945	1.036 (0.784 to 1.369)	0.803
High TG	0.785 (0.623 to 0.989)	0.040*	0.944 (0.622 to 1.432)	0.785	0.734 (0.551 to 0.977)	0.034*
High LDL-C	1.009 (0.774 to 1.315)	0.948	0.721 (0.385 to 1.351)	0.308	1.074 (0.797 to 1.448)	0.638
Low HDL-C	1.009 (0.759 to 1.341)	0.951	0.957 (0.518 to 1.767)	0.887	1.022 (0.737 to 1.418)	0.638
Female						
High TC	1.008 (0.808 to 1.257)	0.944	1.057 (0.766 to 1.460)	0.735	1.225 (0.982 to 1.528)	0.072
High TG	1.067 (0.881 to 1.292)	0.506	0.901 (0.629 to 1.291)	0.571	1.152 (0.915 to 1.450)	0.229
High LDL-C	1.282 (1.040 to 1.581)	0.020*	1.830 (1.119 to 2.991)	0.016*	1.165 (0.922 to 1.473)	0.201
Low HDL-C	0.830 (0.577 to 1.194)	0.316	1.231 (0.660 to 2.298)	0.513	0.797 (0.504 to 1.260)	0.331

*p<0.05; **p<0.01.
Model 1: crude model. Model 2: adjusted model (adjusted variables: age, education level, marital status, eating animal fat, hypertension, diabetes, physical and cognitive activities).
CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; OR, odds ratio; TC, total cholesterol; TG, triglyceride.

male subgroup (OR: 0.679, 95% CI: 0.544 to 0.847, p=0.001) and urban male subgroup (OR: 0.633, 95% CI: 0.483 to 0.823, p=0.001).

After controlling for age, education level, marital status, physical exercise, intellectual activity, eating animal fat, hypertension, diabetes and cerebrovascular disease in model 2, there was no significant correlation between high TC, high TG, high LDL-C, low HDL-C and cognitive impairment. However, gender-stratified multivariate analysis indicated that in the male subgroup, high TG was negatively associated with cognitive impairment (OR: 0.785, 95% CI: 0.623 to 0.989, p=0.040), while high LDL-C increased the risk of cognitive impairment in the female subgroup (OR: 1.282, 95% CI: 1.040 to 1.581, p=0.020). In the urban-rural stratified multivariate analysis, the results were similar to those in the total sample, and there seemed to be no correlation between the serum lipid indexes and cognitive impairment. Both gender-stratified and urban-rural stratified multivariate analyses showed that high TG reduced the risk of cognitive impairment in the urban male subgroup (OR: 0.734, 95% CI: 0.551 to 0.977, p=0.034). High LDL-C increased the risk of cognitive impairment in the rural female subgroup (OR: 1.830, 95% CI: 1.119 to 2.991, p=0.016). However, no significant correlation was found between the remaining serum lipid parameters and cognitive impairment.

DISCUSSION

Main findings

The correlation between lipid profiles and cognitive function remains controversial because of conflicting results from different studies. We speculated that this inconsistency is related to gender and urban-rural regions. Thus, we investigated the gender and urban-rural-dependent association of serum lipid levels with the prevalence of cognitive impairment among community-dwelling older adults. The results of this study show that the prevalence of cognitive impairment in rural area adults aged 65 years and above was significantly higher than in urban areas (35.8% vs 25.2%), which resulted in an overall higher prevalence than a previously published national survey.[30] Our data could also suggest that the prevalence of cognitive impairment among older adults in China is increasing. Additionally, this study found that the correlation between blood lipids and cognitive impairment was different between different genders and urban-rural regions. High TG levels reduced the risk of cognitive impairment in older men, while high LDL-C levels increased the risk of cognitive impairment in older women in fully adjusted models. Further, in the rural female group, the correlation was positive between LDL-C and cognitive impairment, while in the urban male group, the correlation was negative between high TG and cognitive impairment. But no correlation was found between serum lipid levels and cognitive impairment in other groups. These results show that serum lipid levels in older adults are closely related to cognitive impairment with differences in gender and urban-rural residence.

A number of prospective studies found no significant associations between cognitive impairment and TC, LDL-C, HDL-C and triglycerides,[31 32] but none of those studies considered gender or region stratifications. One study based on a rural population indicated that high LDL-C in older women is a risk factor for cognitive impairment.[12] However, a study in Shanghai reported that high levels of LDL-C were inversely associated with dementia and were a potential protective factor against cognitive decline.[33] Goh and Hart found high TG levels were positively associated with short-term memory in Asian men.[34] One study showed that triglycerides levels were associated with a decreased risk of Alzheimer's disease in women.[35] Another study found that high TG levels were negatively correlated with cognitive function in female patients with major depressive disorders.[36] Results of the previous research reported that the relationship between serum lipid levels and cognitive impairment remains unclear. Inconsistencies could result from heterogeneity in study design and sample characteristics, as well as the diagnostic criteria for cognitive impairment. Therefore, in order to clearly explore the relationship between blood lipids and cognitive impairment, stratification analysis according to gender and urban-rural areas was conducted in this study. To our knowledge, this is the first comprehensive subnational assessment of the association between serum lipid and cognitive impairment in Central China to include data on gender and urban-rural areas. We demonstrated that there are gender and urban-rural differences in the correlation of serum lipids with cognitive impairment.

One possible reason for these differences in lipids and cognitive impairment is that in rural areas, older adults have a lower education level and there is a higher rate of hypertension. In urban areas, older adults have a relatively high level of education, healthy lifestyles (less smoking and drinking and more physical activities) and better health conditions (lower ratio of hypertension and diabetes).[37] However, significant urban-rural differences remained between the serum lipid parameters and cognitive impairment in the adjusted model 2. This suggests that rural-dwelling older adults should be considered a priority for the prevention of cognitive impairment.

Gender-specific associations between lipids and cognitive function may depend on genetic vulnerability to dyslipidaemia in men and hormonal status in postmenopausal women.[38] Broader support can be taken from studies of sex differences in serum lipid patterns. For example, fat moves twice as fast through the bloodstream in women as it does in men.[39] Furthermore, age-graded changes in serum lipids occur earlier in men than in women.[39] The physiological underpinning of these gender differences remains speculative. Different levels of sexual dimorphism have been reported for different lipid traits based on cholesterol fractions.[40] An animal study has suggested sex differences are linked to a difference in LDL receptors.[41] Therefore, different strategies should be developed for men and women.

Currently, there are very few studies on the direct association between cognitive function and serum lipids. Some think serum lipids, especially triglyceride, may be a meaningful indicator of nutritional status.[42] Triglyceride can increase the blood–brain barrier transport of insulin, which can improve cognitive function.[43] Additionally, higher serum triglyceride indicates an abundance of circulating fatty acids that can protect cognitive function and decrease dementia risk.[44] Low triglyceride concentrations were correlated with brain inflammation, frailty and low nutrition levels. Low triglyceride levels may, in turn, reflect a low nutritional-level diet, implying pathological changes, or they may be a marker for early cognitive impairment.[45] High concentrations of TC and LDL-C have been proven to be independent risk factors for cerebrovascular diseases, which may, in turn, result in cognitive impairment through cerebral ischaemia.[46] Meanwhile, high TC and LDL-C levels may also be connected with small-vessel diseases by holding a vital role in maintaining the balance of cholesterol levels in the brain. Thus, high TC and LDL-C could promote cognitive impairment through a cerebrovascular pathway.[47] However, the reasons for these relationships remain to be clarified.

Limitations

This study has certain limitations: (1) This is a cross-sectional study, so it cannot establish a causal relationship between lipid level and cognitive impairment. Future cohort studies will be designed to further explore the causal relationship between blood lipid levels and cognitive impairment. (2) The results cannot be generalised to the whole population in China because the sample population was selected from one province. (3) Some factors, such as physical exercise, sleep and medication, may affect lipid levels. Therefore, field measurements may not be a good representation of the true levels of lipids. (4) There may be some bias in the results due to the exclusion of people with dementia from the initial study population selection. Therefore, the findings cannot be generalised to the whole population and readers should be aware of these limitations. We will explore the characteristics of these excluded groups further in future studies.

Implications

This study suggests that there are gender and urban-rural differences in the correlation of serum lipids with cognitive impairment. Specifically, high triglyceride levels may be a protective factor for cognitive function in older urban men, while high LDL-C levels may be a risk factor for cognitive function in older rural women. These results suggest that gender-specific and region-specific effects should be taken into account when assessing the relationship between lipids and cognitive impairment. In addition, multicentred population-based studies with larger sample sizes are needed to verify whether changes in serum lipids lead to changes in cognitive performance. Therefore, the findings of this study should be considered preliminary and further studies are needed to validate and confirm them.

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