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Original Research Article

Associations between GAD/depression and stroke and dyslipidemia among middle-aged and old rural residence in Bayannaoer, China

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- Generalized anxiety disorder
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Abstract

Background: Generalized anxiety disorder (GAD) and depression are well documented as common for middle-aged and old people, yet the evidence on their relationship with stroke and dyslipidemia is not definite. To evaluate the association between GAD/depression and stroke and dyslipidemia among middle-aged and old rural residence in Bayannaoer.

Methods: Data were collected from the cross sectional survey among middle-aged and old rural residence in Bayannaoer via face-to-face interviews. Multivariate logistic regression analyses were conducted to assess the associations between GAD/depression and stroke and dyslipidemia independent from the interaction among GAD and depression.

Results: Of 832 middle-aged and old rural residences in Bayannaoer, 3.37% and 15.38% of the participants were diagnosed with stroke and dyslipidemia by the hospital of county level or above, separately. The adjusted odds ratio (AOR) per 1 higher GAD score for stroke was 1.12(95% confidence interval [CI], 1.04-1.20); and dyslipidemia, 1.07 (95% CI, 1.02-1.11).The AOR per 1 higher depression score for stroke and dyslipidemia were 1.12 (95% CI, 1.04-1.21) and 1.04 (95% CI, 1.00-1.09) respectively.

Conclusions: GAD/depression score was positively associated with stroke and dyslipidemia independently among middle-aged and old rural residence in Bayannaoer. Interventions should be taken to reduce GAD/depression and prevent stroke and dyslipidemia among middle-aged and old rural residence.

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death worldwide in recent years [1, 2]. The morbidity and mortality of CVD has rapidly increased since the late 1980s, and accounts for up to 40% of all deaths among rural and urban populations in China [3,4]. Stroke is one of the major types of cardiovascular diseases, which is also including dyslipidemia. In addition, dyslipidemia is a key determinant of atherosclerosis, which is closely associated with stroke.

Generalized anxiety disorder(GAD) is the most common anxiety disorder [5], which include variety of psychological and physical discomfort, such as autonomic nervous arousal, restlessness, fatigue, inattention, irritability and insomnia [6]. The 12-month prevalence rate of GAD has been estimated to be between 1.2 and 1.9% and the lifetime prevalence between 4.3 and 5.9% [7]. Depression is a mood disorder characterized by listlessness and slow thinking, which can be accompanied by psychomotor retardation symptoms including a loss of interest in normal activities [8]. A meta-analysis revealed that the pooled prevalence of depression in menopausal Chinese women was 36.3% [9].

Anxiety and depression are common symptoms of post-stroke [10, 11]. Anxiety disorders was associated with a significantly increased risk of stroke with an overall hazard ratio of 1.24 [12],

whereas there was no direct evidence about GAD. Depression is also a common complication of stroke and may aggravate the process of neurological diseases after stroke, enhance the sense of helplessness of patients, further reduce the quality of life of patients, significantly reduce the effectiveness of treatment and rehabilitation measures, and increase the risk of death [13]. There is evidence suggests that the risk of stroke increases shortly after the diagnosis of anxiety disorders, while patients with severe anxiety disorders may have a higher risk of stroke [12]. A cohort study of 401,219 participants showed that the hazard ratio per 1-SD higher depression score for stroke was 1.10 [14].There are also some studies showed GAD and depression are particularly associated with dyslipidemia and had an adverse relation with dyslipidemia [15-18]

Even though the link between anxiety/depression and stroke has been established, but the interaction between GAD and depression was uncovered, if it is existed, what about the independence effect on stroke? Evidence of association between GAD/depression and stroke/dyslipidemia was even more limited in China.

Hence, we conducted a cross-sectional study among middle-aged and old rural people in Bayannur, Inner Mongolia, to explore the effect of GAD/depression and the interaction between them on stroke, dyslipidemia independently.

METHODS

Study population

A cross-sectional survey was conducted among residents in rural area of Bayannaoer city in 2016 and 2018. Firstly, according to whether arsenic in drinking water>10 ug/L, all the villages were divided into two layers, then, villages were selected from these two layers. Fourteen villages in Bayannaoer city were selected, among them. 8 villages (Defeng, Gaofeng, Chunguang, Taihua, Tairong, Xinjian, Mantianhong and Wufeng) were supplied with water arsenic concentration>10 μg/L, and the other 6 villages (Zhongnanqu, Guanglian, Nongguang, Xiqu, Rongfeng and Huangchai) were covered by improvement wells, with water arsenic concentration <10 μg/L. All adult residents in these fourteen villages were invited for eligibility screening. Those who were 45 years or older, lived in study villages for at least 10 years, and provided consent were eligible and enrolled in the study. This study was approved by the institutional review board of Baotou Medical College (Baotou medical college IRB 2018 No. [001])

Data collection

Data was collected via face-to-face interviews conducted by trained interviewers including age, gender, ethnicity, education, marital status, number of family member, occupation, duration of living in study sites, smoking habit, sleep onset latency (time taken to fall asleep) , feeling financial pressure; GAD and depression symptoms in the last 2 weeks; stroke and dyslipidemia.

GAD was measured using the GAD-7 scale, which has seven items on the symptoms of GAD over the last 2 weeks. Participants were asked the frequency of the symptoms in the past 2 weeks using a scale of 0 for 'nearly no,' 1 for 'less than a half days,' 2 for 'more than a half days' and 3 for 'nearly all days'. A sum score is calculated by adding the answers of all items on a four-point Likert scale (0–3), ranging from 0 to 21. The scores of 0-7, 8-10 and 11 or more are categorized as normal, borderline and likely anxiety, respectively [19]. The cronbach's alpha of GAD-7 was 0.86.

Depression was assessed using the Center for Epidemiologic Studies Depression Scale-10 (Chinese version) [20]. The Cronbach's alpha of it was 0.64. It's a 10 items scale which was derived from the original version of 20-item CESD. Participants were asked the frequency of the symptoms in the past week using a scale of 0 for 'less than a day,' 1 for '1–2 days,' 2 for '3–4 days' and 3 for '5–7 days'. A sum score is calculated by adding the answers of all the 10 items, ranging from 0 to 30, a higher score indicating a higher level of depression. The scores of 10 or more are categorized as clinically depression [21].

Stroke and dyslipidemia were diagnosed by hospitals above the county level based on well-accepted international standards. Stroke was defined as an acute-onset of focal (or global) neurological deficit lasting >24 hours without an apparent nonvascular origin [22]. Dyslipidemia was defined as having at least one of the following : TC≥ 5.18 mmol/L, LDL-C ≥ 3.37 mmol/L, TGs ≥ 1.70 mmol/L, and HDL-C < 1.04 mmol/L , or using an antilipidemic medication [23].

Statistical analysis

The primary dependent variables were stroke, dyslipidemia. The main predictors of the dependent variables were GAD/depression, which were used as both continuous and dichotomous. As used as dichotomous, GAD was categorized as normal, borderline and likely anxiety, depression was classified into two categories. Simple descriptive statistics (proportion, mean, standard deviation [SD] and so on) for the main outcomes and predictors were calculated. Univariate logistic regression models were used to evaluate the associations between GAD/depression and stroke and dyslipidemia. In addition, multivariate logistic regression models were performed to assess the associations between GAD/depression and stroke and dyslipidemia while adjusting for variables associated with GAD and depression. Considering the possible interaction between GAD and depression, we further ran the model with an interaction term to see whether there is an interaction, if there was, it was adjusted. Statistical analysis was performed with SAS (SAS 9.4; SAS Institute, Inc., Cary, NC).

RESULTS

Demographic and behavioral characteristics

Of 832 rural residence in Bayannaoer, the majority were aged 56-86 (59.62%), female (60.41%), han ethnic (98.44%), primary school or below educated (56.49%), married currently (91.59%), living with family(94.59%), farmers (94.11%), living in local 30 years or more (89.78%). More than one quarter of them had the habit of smoking (28.74%). 20.43% of them used more than 30 minutes to fall asleep. Nearly half of them reported financial pressure (45.13%) (Table 1).

Table 1: GAD and depression of 832 participants in Bayannaoer City in northern China, 2016.

Variable	n (%)	GAD		depression	
		Score	*P*	Score	*P*
Age group in years			0.092		0.123
45-55	336(40.38)	3.81±4.51		4.42±4.94	
56-86	496(59.62)	3.28±4.26		4.97±4.99	
Gender			<0.001		<0.001
Male	329(39.59)	2.33±3.72		3.62±4.17	
Female	502(60.41)	4.25±4.60		5.48±5.32	
Ethnic			0.316		0.770
Others	13(1.56)	4.75±3.82		5.17±3.61	
Han	819(98.44)	3.47±4.37		4.74±5.00	
Education			0.096		<0.001
Middle school or above	362(43.51)	3.20±4.17		4.03±4.36	
Primary school or below	470(56.49)	3.72±4.50		5.29±5.35	
Marital status			0.987		<0.004
Others	70(8.41)	3.49±4.55		6.40±5.14	
Married currently	762(91.59)	3.49±4.35		4.60±4.94	
Number of family member			0.005		0.757
<2	45(5.41)	1.67±2.25		4.98±4.71	
≥ 2	787(94.59)	3.60±4.43		4.74±5.00	
Occupation			0.439		0.913
Others	49(5.89)	3.02±3.61		4.83±4.27	
Farmer	783(94.11)	3.52±4.41		4.74±5.02	
Living in local			0.339		0.150
10-30 years	85(10.22)	3.93±4.48		3.99±4.82	
≥ 30 years	747(89.78)	3.44±4.35		4.83±4.99	
Smoking habit			0.023		0.271
No	590(72.26)	3.71±4.47		4.86±4.99	
Yes	238(28.74)	2.93±4.01		4.43±4.88	
Sleep onset latency			<0.001		<0.001
≤30min	662(79.57)	3.12±4.11		3.97±4.42	
>30min	170(20.43)	4.96±5.01		7.86±5.80	
Feeling financial pressure			<0.001		<0.001
No	456(54.87)	2.28±3.72		3.21±3.81	
Yes	375(45.13)	4.92±4.60		6.59±5.50	

Distributions of depression and anxiety

The mean score of GAD among the study population was 3.49 (SD:4.37) on a scale of 0–21. Of 832 participants, 85.46% (711) were classified as "likely" anxiety, 6.85% (57) as "borderline" anxiety and 7.69% (64) as "normal". The mean score of depression among the study population was 4.75 (SD: 4.98) on a scale of 0–30. 14.78% (123) were categorized as clinically depression. Totally 3.37% and 15.38% of the participants were diagnosed with stroke and dyslipidemia by the hospital of county level or above, separately. Crude analyses suggested that 'likely GAD' and clinical depression were higher among participants with diagnosed stroke and dyslipidemia, 'borderline GAD' were higher among participants with diagnosed dyslipidemia (Table 2).

Associations between GAD/depression and stroke and dyslipidemia

The simple logistic regression analysis showed that participants with "likely" GAD/clinically depression was more likely to be diagnosed with dyslipidemia; GAD and depression score were positively associated with stroke and dyslipidemia. The interaction of GAD and depression was statistically associated with dyslipidemia in the univariate modeling.

After adjusted for adjusted for age group, gender, number of family member, smoking, sleep onset latency, and feeling financial pressure, "likely" GAD was associated with a threefold increase in the odds of stroke (AOR: 4.00, 95% CI: 1.34-11.96)

Table 2: Scores of generalized anxiety disorder and depression by chronic disease among 832 participants (n/%).

chronic disease	Total sample	GAD			Depression	
		Normal	Borderline	Likely	Normal	Clinically
Stroke						
No	804(96.63)	689(85.70)	56(6.97)	59(7.34)	687(85.45)	117(14.55)
Yes	28(3.37)	22(78.57)	1(3.57)	5(17.86)	22(78.57)	6(21.43)
Dyslipidemia						
No	704(84.62)	616(87.50)	45(6.39)	43(6.11)	614(87.22)	90(12.78)
Yes	128(15.38)	95(74.22)	12(9.38)	21(16.41)	95(74.22)	33(25.78)

; the odds of stroke increased by 12% (AOR: 1.12, 95% CI: 1.04-1.21) as GAD score increased by one unit.

After adjusted for age group, gender, education, marital status, sleep onset latency , and feeling financial pressure, along with the depression score increased by one unit, the odds of stroke increased by 12% (AOR: 1.12, 95% CI: 1.04-1.21).

After adjusted for age group, gender, marital status, number of family member, smoking, sleep onset latency, feeling financial pressure, and the interaction between GAD and depression, "likely" GAD (AOR: 4.71, 95% CI: 1.88-11.44) and clinically depression (AOR: 2.55, 95% CI: 1.26-5.00) was associated with a 371% and 155% increase in the odds of dyslipidemia; as GAD score increased by one unit, the odds of dyslipidemia increased by 7% (AOR:1.07, 95% CI: 1.02-1.11); as depression score increased by one unit, and the odds of dyslipidemia increased by 4% (AOR:1.04, 95% CI: 1.00-1.09).

The variable was significant at 0.05 level; AOR: adjusted odds ratio; A: adjusted for age group, gender, number of family member, smoking, sleep onset latency, and feeling financial pressure; B: adjusted for age group, gender, education, marital status, sleep onset latency , and feeling financial pressure; C: adjusted for age group, gender, marital status, number of family member, smoking, sleep onset latency , feeling financial pressure, and the interaction between GAD/depression. (Table 3)

DISCUSSION

In the current study, after adjusted for potential confounders, such as age, gender, sleep and financial pressure, we found that in the middle-aged and old rural residence in Bayannaoer, GAD score/depression score and stroke/dyslipidemia independently. Higher GAD score indicated significantly increased odds of diagnosed stroke and dyslipidemia. Higher depression score indicated significantly increased odds of diagnosed stroke and dyslipidemia independently, which could explain by GAD and depression increasing inflammatory factors (interleukins 6 and 1β, tumour necrosis factor α and C-reactive protein), resulting in cardiovascular disease [24]. Our result was in consistent with the research results that anxiety disorders [12] and depression [14] increased risk of stroke with an overall hazard ratio 1.24 and 1.10, respectively. Data support a strong causal link of GAD and depression to insomnia [25, 26], further, insomnia increased the risk of ischemic stroke [27, 28]. There was interaction between GAD and depression when we assessed the effect of GAD/depression on dyslipidemia, after adjusted the interaction, there were positive associations between them independently. The evidence on the association between GAD and dyslipidemia is sparse, but adverse effect of anxiety [17] and depression [17, 18] on dyslipidemia have been found. Results in rats also supported the relationship between the symptoms of depressive/anxiety and dyslipidemia [29].

Table 3: Association between generalized anxiety disorder and depression and chronic disease.

Covariate	Stroke		Dyslipidemia	
	OR (95% CI)	AOR (95% CI)	OR (95% CI)	AOR (95% CI)
GAD				
Normal	1.0	1.0	1.0	1.0
Borderline	0.56(0.07,4.23)	0.69(0.09,5.33) [A]	1.73(0.88,3.39)	1.52(0.70,3.10) [C]
Likely	2.65(0.97,7.26)	4.00(1.34,11.96)*,[A]	3.17(1.80,5.57)*	4.71(1.88,11.44)*,[C]
GAD score	1.08(1.00,1.15)*	1.12(1.04,1.20)*,[A]	1.09(1.05,1.13)*	1.07(1.02,1.11)*,[C]
Depression				
Normal	1.0	1.0	1.0	1.0
Clinically	1.60(0.64,4.03)	1.86(0.67,5.15) [B]	2.37(1.51,3.73)*	2.55(1.26,5.00)*,[C]
Depression score	1.08(1.01,1.15)*	1.12(1.04,1.21)*,[B]	1.07(1.03,1.11)*	1.04(1.00,1.09)*,[C]
GAD*Depression	0.62(0.19,2.09)	0.62(0.20,2.15)	0.47(0.25,0.88)*	0.41(0.22,0.79)*,[C]
GAD score* Depression score	1.00(0.99,1.01)	1.00(0.99,1.01)	1.00(0.99,1.00)	1.00(0.99,1.00)

It remains unclear whether GAD/depression precedes or follows stroke and dyslipidemia, or if they co-occur. But, it was observed that higher depression score at the baseline was significantly increased the incidence of stroke and CVD [14], anxiety disorders at baseline also significantly increased risk of stroke [12]. Further, mixed methods research is needed to provide more critical information about the pattern of GAD/depression and CVD with middle-aged and old rural residence in Bayannaoer.

In the current study, the diagnosed rates of stroke among middle-aged and old rural residence in Bayannaoer was 3.4% , which was higher than those (1.7%) reported by study of Li *et al.*, which investigated 4979 residents in rural areas of Yun Nan province [30]. The diagnosed rates of dyslipidemia was 15.4%, which was lower than 42.65% in migrants in Inner Mongolia in 2020 [31], the possible reason may be that diagnosed rate of dyslipidemia was lower estimated since rural residents without clinical symptoms will not be regularly test for blood lipid in Bayannaoer.

There are some limitations in this study: firstly, the sequence between stroke and dyslipidemia and GAD/depression disorders from cross-sectional study cannot be distinguished, so it is difficult to infer the causal relationship between them. Secondly, the rate of stroke and dyslipidemia were calculated based on the diagnosis of hospital above county level. The rate of illness may be underestimated because that some people with corresponding illness did not go to the hospital for diagnosing. However, our study had special characters: first, we focused on the most common type of anxiety disorder and its impact on stroke and dyslipidemia among middle-aged and old rural residence in Bayannaoer; second, we took the interaction of GAD and depression into consideration, found that GAD and depression score were independently associated with dyslipidemia; three, we controlled for financial pressure and sleep onset latency, which may associated with GAD/depression [32] and CVD [28].

This study, demonstrated that in the middle-aged and old rural residence in Bayannaoer, GAD/depression was associated with stroke and dyslipidemia independently. Patients with stroke and dyslipidemia, which leads to the decline of life quality, may be perplexed with negative emotions inevitably. Moreover, anxiety and depression may aggravate the corresponding disease. So the government should focus on the GAD and depression disorder and stroke and dyslipidemia, and people should also improve their ability to identify anxiety/depression and then effective measures should be taken to control them.

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ETHICAL APPROVAL

This study was approved by the institutional review board of Baotou Medical College. (No.2018 (001))

STATEMENT OF HUMAN AND ANIMAL RIGHTS

All procedures in this study were conducted in accordance with the institutional review board'S (No.2018 (001)) approved protocols.

STATEMENT OF INFORMED CONSENT

Written informed consent was obtained from the patients for their anonymized information to be published in this article.

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