Original Research Article

Gender-based clinical study on the association of cognitive impairment with drinking and smoking

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Abstract

Purpose: To evaluate the relationship between alcohol consumption and cigarette smoking among the elderly population of a Chinese city with a risk of developing cognitive decline and dementia.
Methods: In this study, 1687 participants from the suburban town of Yanliang in Xi'an Sub-province, Shanxi Province, China in the age group of 60 - 65 years and who have not develop cognitive decline were assessed over a 6-year period. The study involved the evaluation of gender-based effect on alcohol consumption and smoking cigarette and its impact on cognitive functions.
Results: The study observed that smokers have a higher risk of cognitive decline than non-smokers (odds ratio = 1.51; 95 % CI = (1.07 – 2.11). Interestingly, the odds ratio of the smokers among the female subjects was 1.54; 95 % CI (1.02 - 2.49) compared to female non-smokers. Moreover, a dose-dependent relationship was observed for those female smoker with higher pack-years compared to non-smokers (p = 0.003). On the other hand, regular alcohol consumption also increased the possibility of dementia and cognitive decline (odds ratio = 1.69; CI at 95 % = (1.03 – 2.75), hence a dose-dependent relationship was observed between male users (p = 0.042).
Conclusion: The results suggest that alcohol consumption and smoking are linked with cognitive decline among the female subjects in the age group of 60 – 65 years. Thus, the relationship between these factors is characterized by gender difference which may be due to female sex hormones.

Keywords: Cognitive health, Alcohol consumptions, Smoking, Elderly population

INTRODUCTION

The population of the Chinese people which is ≥ 65 years constitutes around 15 % as per 2010 census [1]. The number of these elderly populations is increasing day by day. Thus, a social burden comprising of cognitive health issues such as dementia, loss of cognitive functions, sensory impairments, malnutrition, physical injury has become an important issue [2]. Among the elderly Chinese population, cognitive decline or cognitive impairment is the major health issue [2]. Thus, there is an urgent need for checking the development of cognitive impairment among these elderly populations which can be prevented by identifying the changeable risk factors. Additionally, there are various reports that suggest dementia or

cognitive decline in aged population is associated with smoking and alcohol consumption [2,3]. In fact, the association of cognitive impairment between drinking alcohol and smoking is widely discussed during the recent years. On the contrary, there are also reports which suggest that nicotine improves short-term cognitive performance by inhibiting the amyloid formation [3]. In addition, Xu et al reported that moderate consumption of alcohol protect against dementia while excessive consumption increases the risk for dementia [4]. When it comes to the gender difference in the elderly population, women constitute half of the smokers [5,6]. Hence, gender difference is an important factor while studying the health effects of the cognitive decline. Although many studies have reported on the health effects related to smoking and alcohol consumption and its association with cognitive decline, several studies lack to focus and report on the gender differences [7-9]. In fact, many researchers failed to report on the physical and social health that is linked with cognitive decline during the follow-up period [7-10]. However, the association between smoking and cognitive decline is still in the debate and controversial [8,9]. Therefore, the present study aim at the prospective study of the elderly Chinese Community population to assess the association between alcohol consumption and smoking and cognitive decline during a 6 year study period. The present study is an attempt to evaluate the gender-based association of cognitive impairment between smoking status and alcohol consumption.

METHODS

Compliance with ethical standards

The protocol was approved by the Institutional Ethical Committee vide Ref No.SPPH/EthicsAnim/2016/07/25A. All procedures were performed in accordance with the 1964 Helsinki Declaration and its later amendments or similar ethical standards [11]. Informed consent was also obtained from all the individual participants included in the investigation. Verbal informed consent was taken from the illiterate participants. Therefore written consent was also taken from the parents or guardians of these participants. Verbal interviews and personal interviews were carried out by the experienced medical students and practitioner.

Study population

Data were obtained from the inhabitants of the suburban town of Yanliang under Xi'an sub-province, Shanxi Province, China, which has a population of 150,130. The study subjects were aged 60 - 65 years and the study area covers around 436.13 square km. The study subjects were identified based on community resident information and registration from the Community Information Center. Their actual date of birth was cross-checked for verification purposes. Follow-up evaluations were started in 2010 and completed in 2016. A total of 2034 participants volunteered in the evaluation; however, 348 participants were not available for further evaluations. Hence, 1687 participants took part in the follow-up period.

Data collection

Data collection was carried out based on personal interviews with experienced medical personnel, doctors and students. The volunteers/participants were briefly described about the main purpose of the survey. Finally, screening was carried out for cognitive impairment and depressive symptoms for those participants who were willing to take part in the program. Their daily activities, lifestyle and marital status, education were also recorded (Table 1). The questionnaire used in the follow-up period was recorded for their smoking status. The status includes whether the participant is a present-smoker, ex-smoker or a non-smoker.

The details of smoking duration and number of cigarettes smoked per day were obtained from the present-smoker and ex-smoker. Based on the equation developed by Park *et al* [12] they were classified into two categories: high (≥ 50 %) and low (< 50 %). Similarly, the questionnaire used in the follow-up period for the alcohol consumption status include the details of present alcohol consumption and its rate of consumption. The study subjects were further classified as non-drinker, moderate-drinkers (1 to 4 times per week), and regular-drinkers (more than 4 times per week). Global cognitive functioning was evaluated and measured with a modified version of the Mini-Mental State Examination-Chinese (MMSE-C) [13].

The content was mostly translated literally without any deviations from the original questionnaire. Some questions were modified to adjust with the cultural criteria for Chinese tradition [13]. Cognitively impaired subjects were classified as those participants who scores MMSE-C ≤ 24. GD (Geriatric Depression) Scale was used for assessing the depression and the instrumental activities of daily living (IADL) was measured in terms of Lawton Scale.

Table 1: Baseline gender-based socio-demographic characteristics of the study subjects

Characteristic		Male (n (%) = 748)	Female (n (%) = 939)	P-value
Marital status	Married	723 (96.66 %)	594 (63.26%)	< 0.002
	Single/widowed/ divorced	18 (2.41)	345 (36.74%)	
Cohabitants				
	Single or Lone smoker	9 (1.20)	111 (11.82)	< 0.002
	Dual with one partner	321 (42.91)	394 (41.96 %)	
	2 or more	193 (25.80)	169 (18.0 %)	
	More than 3 or in groups	225 (30.08)	265 (28.22 %)	
Employment status				
	No	124 (15.24)	325 (34.61 %)	< 0.001
	Employed	634 (84.76)	645 (68.69)	
Smoking				
	Never-smokers	119 (15.91)	808 (86.05 %)	< 0.001
	Ex-smoker	214 (28.61)	18 (1.92)	
	Present-smoker	415(55.48)	113 (12.03)	
Drinking				
	Never drunk	178 (23.80)	812 (85.65)	< 0.001
	Ex-drinker	99 (13.24)	19 (2.0)	
	Current drinker	471 (62.97)	117 (12.34)	
Hospitalization in past year				
	No	212 (28.34)	149 (15.87)	< 0.001
	Yes	536 (71.66)	790 (84.13)	
Depressive symptom				
	No	634 (84.76)	696 (74.12)	<0.002
	Yes	114 (15.24)	243 (25.88)	
IADL impairment				
	No	677 (90.51)	618 (65.81)	< 0.001
	Yes	71 (9.49)	321 (34.19)	
MMSE-C score	Mean (SD)	27.4 (1.3)	26.3 (1.4)	< 0.002

Data analysis

Statistical analyses were carried out using the IBM SPSS Statistics 20 (SPSS, Inc, USA). The socio-demographic characteristics of the 1687 participants without cognitive decline are described in percentage and amount. The chi-square test was used to evaluate the social and demographic characteristics of the subjects which develop cognitive decline as well as those subjects which did not develop cognitive decline. Multiple logistic regressions (MLR) analysis was carried out to evaluate the independent factors associated with the cognitive decline between smoking and alcohol consumption. The MLR logistic modeling allows to carry out two binary comparisons simultaneously. Within each comparison, the odds ratio (OR) and confidence interval (95 %), was calculated by comparing to a control group. The control group was considered as an index of the relationship between cognitive decline and smoking/alcohol consumption. The control groups in this study are the non-drinkers and non-smokers.

Gender-based evaluations were carried out on the levels of smoking and alcohol consumption which may be the reason for developing cognitive decline during the 6 years follow-up.

The dose-dependent relationship was evaluated for determining the P for trend. The trend test was carried for estimating the amount of smoked cigarettes in packets per year and the total amount of alcohol consumption per week. Statistical analyses were adjusted for gender-based analysis, drinking and smoking co-habitants, MMSE-C score baseline, IADL impairment, and the status of smoking and alcohol consumption.

RESULTS

Table 1 shows the gender-based social, clinical and demographic characteristics of the volunteered elderly population. The results observed a significant difference in the male-female characteristics distribution. The comparative analysis of the male-female gender based on socio-demographic characteristics on the development of cognitive decline is shown in Table 2.

Table 2: Socio-demographic characteristics of the study subjects at baseline based on the development of dementia and cognitive decline

Characteristic		Participants without dementia and cognitive decline at follow up (n (%) =1138)	Participants with dementia and cognitive decline at follow up (n (%) =549)	*P*-value
Gender				
	Male	621 (54.57)	143 (26.05)	< 0.002
	Female	517 (45.43)	406 (73.95)	
Marital status				
	Married	971 (85.33)	404 (73.59)	< 0.001
	Single/ widowed/ divorced	167 (14.67)	145 (26.41)	
Cohabitants				
	0	66 (5.80)	57 (10.40)	< 0.002
	1	491 (43.15)	247 (45.07)	
	2	249 (21.88)	95 (17.34)	
	3 or more	332 (29.17)	149 (27.19)	
Employment status				
	No	263 (23.11)	144 (26.23)	< 0.021
	Employed	875 (76.89)	405 (73.77)	
Smoking				
	Never	09 (53.51)	351 (63.93)	
	Ex-smoker	180 (15.82)	47 (8.56)	
	Present-smoker	349 (30.67)	151 (27.50)	
Drinking				
	Never	629 (55.27)	355 (64.66)	
	Ex-drinker	88 (7.73)	33 (6.01)	
	Current drinker	421 (36.99)	161 (29.33)	
Hospitalization in past year				
	No	245 (21.53)	106 (19.31)	< 0.381
	Yes	893 (78.47)	443 (80.69)	
Depressive symptom				
	No	891 (85.84)	374 (68.12)	< 0.001
	Yes	147 (14.6)	175 (31.88)	
IADL impairment				
	No	898 (86.51)	332 (60.47)	< 0.001
	Yes	140 (13.49)	217 (39.53)	
MMSE-C score	Mean (SD)	27.2 (1.3)	26.5 (1.4)	< 0.001

The study also observed that 549 subjects developed cognitive decline during the six-year study period. Mostly female subjects 406 (73.95 %) developed cognitive decline with a majority being unemployed and consume alcohol. They also tend to possessed symptoms of depression with a lower MMSE-C score ($p < 0.05$).

In Table 3, it is observed that present-smoker have a higher risk of cognitive decline compared to non-smokers (Odds ratio = 1.51; CI at 95 % = 1.07 – 2.11). While the smokers with a low amount of pack-years observed an increased in the odds ratio. Therefore they tend to have a higher risk of developing cognitive decline compared to non-smokers (Odds ratio = 1.56; CI at 95 % = 1.08 – 2.17), as shown in Table 3. However, there was no statistically significant difference between high pack-years smokers and

cognitive decline (OR, 1.28; 95 % CI, 0.84 – 2.01) (Table 3).

The study also observed that the female subjects possessed significant effects of smoking on developing cognitive decline. The odds for the female present-smokers in the development of cognitive decline was 1.51 (CI at 95 % = 1.02 – 2.49) (Table 3) compared to non-smokers. The female subjects who consume a higher packet of cigarette per year were found to be almost doubled the chances of developing cognitive decline compared to non-smokers (Odds ratio = 2.35; CI at 95 % = 1.27 – 4.28). Thus, indicating a dose-dependent relationship ($p = 0.003$).

In Table 4, the association of drinking and its effect on cognitive decline is presented. A non-linear relationship was observed on the association of drinking and cognitive decline.

Table 3: MLR analysis reflecting the progression of smoking status of the participants during their age from 60-65 years on the development of cognitive decline after the 6-year study period

Variable		Total OR	Total CI at 95%	Males OR	Males CI at 95%	Females OR	Females CI at 95%
Baseline Smoking							
	Non-smoker	1	(Control)	1	(Control)	1	(Control)
	Ex-smoker	1.32	(0.85 – 2.11)	1.01	(0.51-1.83)	2.07	(0.71-5.96)
	Present-smoker	1.51	(1.07 – 2.11)	1.23	(0.71-2.19)	1.51	(1.02-2.49)
Number of pack-years							
	Never	1	(Control)	1	(Control)	1	(Control)
	Low	1.56	(1.08 – 2.17)	1.29	(0.74-2.27)	1.25	(0.71-2.14)
	High	1.28	(0.84 – 2.01)	1.15	(0.61-2.15)	2.35	(1.27-4.28)
P for trend (P)		0.342		0.978		0.003	

Table 4: MLR analysis on the progression of alcohol consumption and development of cognitive decline during the 6–year study period

Variable		Total OR	Total CI at 95%	Male OR	Male CI at 95%	Female OR	Female CI at 95%
Baseline-Drinking							
	Non-Drinker	1	(Control)	1	(Control)	1	(Control)
	Ex-Drinker	1.06	(0.64 – 1.76)	1.66	(0.86 – 3.20)	0.62	(0.24 – 1.62)
	Present-Drinker	1.06	(0.79 – 1.43)	1.51	(0.92 – 2.47)	0.83	(0.55 – 1.27)
Amount of drinking per week							
	Never	1	(Control)	1	(Control)	1	(Control)
	Non-Regular	0.89	(0.65 – 1.24)	1.29	(0.75 – 2.23)	0.69	(0.45 – 1.04)
	Regular	1.31	(0.91 – 1.89)	1.66	(1.98 – 2.75)	1.17	(0.54 – 2.59)
P for trend (P)		0.157		0.042		0.611	

The result also observed that regular alcohol consumption has a higher risk of developing cognitive decline (Odds ratio = 1.69; CI at 95 % = 1.03 – 2.75). Among the male subjects, a dose-dependent relationship was established on the association of alcohol consumption and cognitive decline (p = 0.042). But in the case of female non-regular drinkers, there was a lesser chance of developing cognitive decline (Odds ratio = 0.69; CI at 95 % = 0.45 – 1.04).

DISCUSSION

The study observed a significant difference in the development of cognitive impairment in the studied population amongst the male and female population. The study also observed that cognitive impairment was associated with those persons with drinking and smoking habits in their early 60s. Those women who never smoke in their lifetime had a lesser chance of developing dementia and cognitive decline.

The higher risk among the female smokers also suggests that they tend to developed cognitive impairment in a cumulative manner. However, this was different in case of males. There was a non-linear relationship between alcohol consumption and cognitive decline in females. However, among the male subjects, a dose-dependent relationship was observed with respect to alcohol consumption. Thus these subjects have a higher possibility of developing cognitive impairment.

There are several reports on the association of smoking, alcohol consumption and cognitive impairment with different results and views. Nao *et al* observed that smoking is associated with mild cognitive impairment in diabetic patients [14]. On the contrary, Ikeda *et al* observed that smoking diminish the chances of cognitive impairment and the risk for dementia [15]. In addition, Kardani *et al* proposed that the

presence of nicotine in cigarettes activates the nicotinic acetylcholine receptors and stimulates its neuroprotective role and dopaminergic effect [16].

However, recent studies on the magnetic resonance imaging (MRI) of cigarette smoke-related effects on human brain structure have suggested smoking adversely affected the structural integrity of multiple sub-cortical brain regions. Thus increases the chance of dementia, Alzheimer's disease and cognitive decline [17].

A case-control and cohort studies on the association of smoking and Alzheimer's disease showed conflicting results. A meta-analysis of the case-control study suggests that a history of smoking is associated with an increased incidence of Alzheimer's disease especially in those subjects who are current smokers during the follow-up period [18].

Anstey *et al* also reported that current-smokers above 65 years are at the risk of dementia and cognitive decline compared to never-smoker subjects. The workers also suggest that there is not enough parameters and data on determining risk effects of cognitive decline and dementia in ex-smokers or past-smokers. However, their study proposed that cognitive outcomes should be measured in clinical trials [19]. The results of the present investigation observed that our findings are inconsistent with those of the previous study by Durazzo *et al* and Anstey *et al* [18,19]. However, in our study, the chances of developing cognitive impairment in present-smokers were common among the females. However, no significant relationship was observed in the male subjects in terms of cognitive impairment and smoking cigarette [20].

When it comes to gender study, Travis *et al* observed the susceptibility of lung cancer in female smokers because of tar exposure compared to male counterparts [21]. Similarly, our study also suggests that female smokers are more prone in developing cognitive decline compared to male smokers which may be due to the fast rate of nicotine metabolism by the female hormones and its effect on the cognitive decline [22]. Additionally, females exhibited a higher amount of nicotine intake and the total plasma clearance of nicotine is lower compared to males [23].

However, oestrogen which is the primary female sex hormone increases the neuronal function and its neurotransmitter system. Thus, it caused a positive effect on cognitive function [24]. The female subjects in our study possess a low oestrogen level because they are aged above 60 years. Hence, these female subjects developed cognitive decline because of the oxidative stress of smoking and menopause [24]. Also, the oxidative stress caused by smoking deteriorates their cognitive health.

There are also studies which observed that moderate amount of drinking alcohol reduced the risk of dementia and cognitive decline [25] Well these results are in comparison with both non-drinkers and regular-drinker, although there is certain contrasting results [25,26]. Wardzala *et al* reported that moderate use of alcohol reduces the risk of cardiovascular diseases. The beneficial effect may be because of the increase in the prostaglandin I2 thereby inhibiting the platelet activation and thus acts as an effective vasodilator. Wardzala *et al* further reported that men with moderate alcohol consumption experienced an extensive range of beneficial effects associated with alcohol [9].

However, frequent alcohol consumers tend to develop a harmful effect on the cognitive decline because of the neurotoxin from the ethanolic toxic substance. In this study, a direct relation between baseline alcohol drinking and cognitive decline among the studied participants was not observed. But the effects of drinking alcohol associated with cognitive impairment were observed in females. Among the males, there was a consistent relationship between the amounts of alcohol consumption per week and cognitive impairment. On the contrary, there was a low risk of cognitive decline among the females having a moderate level of alcohol drinking. Thus, presenting a non-linear relationship between a moderate level of alcohol drinking and the development of cognitive decline. López-Caneda *et al* also observed that there was a positive relationship between moderate alcohol drinking and cognitive impairment among females and women performed better than men on mental flexibility. On the other hand, their study also observed that men performed better than women on visual processing [27]. In the present study, the standard amount of alcohol consumption was unable to determine because it was measured on weekly basis. Among the females the frequency of alcohol consumption showed a non-linear relationship. However, a direct association was observed in the male subjects that explained the gender-based dissimilar pattern in alcohol consumption.

Limitations of the study

The limitations of the study are that the details of smoking and drinking alcohol were based on

self-reported data. Moreover, the amount of alcohol consumption was measured per week and not on the volume. Lastly, the changes in the smoking and alcohol consumption pattern were not measured in this study.

CONCLUSION

Female smokers in the age group of 60 - 65 years who drink alcohol have the risk of developing cognitive decline and dementia. However, taking into consideration among male and female population and the factors which depend on their lifestyle, further investigation is required with much larger population and sample size. There is also an urgent need for establishing personalized living style modification, food habits and other strategies to prevent cognitive impairment effectively.

DECLARATIONS

Acknowledgement

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Yingying Fu and Xiaoli Chen contribute to this work equally.

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