Socio-demographic and cardiovascular disease risk factors associated with dementia: Results of a cross-sectional study from Lebanon

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Title Page

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Abstract

Little evidence from the Arab region is available on dementia and its associated risk factors. This study is the first in Lebanon to examine the association between community older adults' socio-demographics and cardiovascular disease risk factors (CVDRF) and dementia in the aim of closing the knowledge gap. A cross-sectional household survey was conducted in 2013 in Beirut and two districts of Mount Lebanon with 502 older adults (65 years and above) and their informants. Data was collected on CVDRF and socio-demographics using structured questionnaires and dementia was assessed using the 10/66 Dementia Research Group validated tools. Multivariable analysis was done using a generalized estimating equation to account for cluster effect. Being older and perceiving personal income as insufficient significantly increased the odds of dementia [$OR_{75\text{ -}84\text{ years}}$ =4.00 (95%CI=1.46, 10.95); $OR_{85+\text{ years}}$ =7.07 (1.84, 27.03); $OR_{\text{insufficient income}}$ = 3.90 (1.58, 9.60)]. Having uncontrolled hypertension (versus no hypertension) was the only significant CVDRF that increased the odds of dementia [OR=6.35 (1.60, 25.10)]. Interventions targeting uncontrolled hypertension that aim to increase awareness about proper management of this chronic condition would contribute to the needed preventive efforts against CVDRFs in response to dementia risk. Further research on the association between income sufficiency – one indicator of low socio-economic status – and dementia is warranted.

Key words: Dementia, CVD risk factors, uncontrolled hypertension, income, Lebanon.

Introduction

According to the latest World Alzheimer Report, it is estimated that 47 million people worldwide are living with dementia today, with a projected increase to 75 million by 2030, and 132 million by 2050. The majority of cases (68%) are expected to be living in low and middle-income countries (LMIC) (Prince et al., 2015), where the disease burden profile is being shifted towards more old-age related health conditions and more chronic diseases due to the demographic and health transition. Lebanon is a small upper-middle-income country in the Eastern Mediterranean, with a gross domestic product (GDP) per capita in 2016 of USD 7914, close to Turkey and the average of the Arab region, higher than Iraq, Syria, Jordan and Egypt but lower than Gulf countries (The World Bank, 2017). The proportion of Lebanese older adults (65+ years) is projected to reach 10.2% by 2025 and 26% in 2050 (Sibai et al., 2014), and the average life expectancies recorded in 2015 were 74 and 76 years for males and females respectively (World Health Organization, 2015). Non-communicable diseases (NCD) represent more than 60% of all deaths with a very high burden of cardiovascular diseases (CVD) that accounts alone for 47% of all-cause mortality among all ages and both sexes (WHO, 2014). Lebanon is not different from many middle income Arab countries where Ischemic heart disease and stroke are the leading causes of Disability adjusted life years (DALYs) (Institute for Health Metrics and Evaluation et al., 2013).

Cardiovascular risk factors (CVDRF) play a pivotal role in the etiology of dementia. These are type 2 diabetes mellitus (Mehlig et al., 2014), and midlife high blood pressure (Kennelly et al., 2009), specifically systolic blood pressure (Kivipelto et al., 2001). Behavioral risk factors associated with CVD have been also reported to increase risk of dementia. These are smoking, alcohol, obesity, and physical inactivity (Deckers et al., 2015; Suemoto, 2015). Smoking is of particular importance in the Eastern Mediterranean, including Lebanon where tobacco use is among the highest in the region. Health-related factors such as a family history of dementia, chronic diseases, Parkinson's disease and heart disease have also been associated with a dementia diagnosis at later life (Ertekin et al., 2015).

Published studies have also reported that socio-demographic factors such as increasing age, low socio-economic status, low education, and living in rural areas, are associated with a higher risk of dementia (Arslantas et al., 2009; Ertekin et al., 2015; Yaffe et al., 2013). Incidence studies

have shown no risk differences between males and females (Chene et al., 2015). Yet prevalence studies showed that female gender is associated with higher risk of dementia which could be explained by the higher survival rate of women (Arslantas et al., 2009; Ertekin et al., 2015; Prince et al., 2015).

Knowledge about dementia risk factors, both modifiable and non-modifiable ones, is important for early prevention and implementation of interventions. Data from Lebanon and the region is however scant. The objective of this paper is to examine the association between dementia and various socio-demographic, economic and CVD risk factors among a community-based population of older adults in Lebanon.

Methods

Study Design and Population

This paper is based on data from a cross-sectional population-based study carried in Lebanon in 2013 on a sample of individuals aged 65 and above, residing in Beirut, the capital city, and two main districts of Mount Lebanon, Shouf and Aley. Details of the study are found in Phung et al. (2017). The aim was to assess the burden of dementia and investigate associated factors. The study recruited 508 older adults of whom 502 had complete data on dementia diagnosis hence these were the focus of this study.

A multi-stage cluster sampling was employed in both the capital city and the two districts of the Mount Lebanon governorate. Random clusters were chosen in the targeted areas and within each cluster, households were selected systematically. Trained interviewers door-knocked the selected households and interviewed males and females who were 65 years old or above as well as their identified informants after securing their free and informed consent. The informant was a person identified by the older adult, who knows the latter very well and spends a considerable time with him/her, is the caregiver in case the older adult needs care, and is not a paid helper. The number of older adults aged 65 years or older reached in each governorate was proportional to their size in the Lebanese population.

Data collected from the older adult and his/her informant included indicators necessary to determine dementia diagnosis, socio-demographic characteristics, risk factors, and general health status of the older adult. Out of a total of 802 community dwelling older adults initially approached in the study, 508 consented to participate yielding an overall response rate of 63.3%. Each interview lasted for around two hours. The study was approved by the Institutional Review Board at the American University of Beirut (Protocol Number: FHS.MC.19).

Measures

Assessment of dementia outcome

Dementia was diagnosed using the validated one-stage 10/66 Dementia Research Group (DRG) diagnostic assessment tools which collect data from both the older adult and the informant. These tools include the community screening instrument for Dementia (CSI-D), the modified CERAD (Consortium to Establish a Registry of Alzheimer's Disease) animal naming tests and modified10-word list recall, the Geriatric Mental State (GMS) examination test, the CSI-D informant interview, and the physical assessment and brief neurological examination (NEUROEX). The algorithm, initially developed by Prince et al. (2003), yields a binary outcome for each older adult to assess dementia status. It was recently validated in Arabic with 92.0% sensitivity and 95.1% specificity (Phung et al., 2014).

Assessment of Cardiovascular risk factors

CVDRF included in this paper were: hypertension, diabetes, heart problems, smoking, obesity and physical inactivity.

Information about hypertension, diabetes mellitus and heart problems was self-reported and based on the yes/no question: "have you ever been told by a doctor that you have the condition X?" Furthermore, interviewers trained on using a sphygmomanometer took three consecutive measurements of systolic and diastolic blood pressures from all participants. A participant was classified as non-hypertensive, controlled hypertensive, or uncontrolled hypertensive. A non-hypertensive is a participant who was never been told by the physician that he/she has hypertension. All those who had a history of hypertension were on anti-hypertensive treatment. The 140/90 mmHg cutoff for the mean measures of systolic and diastolic blood pressures was

used to differentiate between controlled (at or below cut off) and uncontrolled (above cut off) hypertension among those diagnosed as hypertensive.

Data were collected on smoking any form of tobacco (cigarettes, cigar, pipe, and water pipe). The most commonly reported one was cigarette smoking. Hence, in this paper, cigarettes pack-year score was used to capture both the intensity and lifetime duration of tobacco exposure. Obesity was assessed using the calculated body mass index (BMI) from measured weight and height of the older adult. BMI was categorized based on the standard World Health Organization groups for underweight (BMI<18.5 kg/m^2), normal weight (BMI 18.5 to 24.9 kg/m^2), overweight (BMI 25 to 29.9 kg/m^2), and obese (BMI $\geq$ 30 kg/m^2). Physical activity was self-assessed using a scale of 1 (very active) to 4 (not at all active). For analytical purposes, the variable was dichotomized (very active or fairly active vs. not active or not at all active).

Assessment of Socio-economic factors

The demographic and socio-economic variables considered for analysis were age, gender, marital status, education, and perception of income sufficiency. Age, originally measured as a continuous variable, was categorized into 65 to 74 years, 75 to 84 years and 85 years and above. Marital status was grouped into currently married vs. unmarried (single, divorced or widowed). Data on education was initially collected using an eight-category variable ranging from illiteracy to university level education which was transformed based on its frequency distribution into a dichotomous variable (formal education including those who went to school, technical institute or university vs. no formal education or no enrollment in any educational system including those who read and write or were illiterate). The participant's self-perceived income sufficiency was assessed using a four-level Likert scale (very sufficient to very insufficient) and reduced to a dichotomous variable (sufficient vs. insufficient) for analysis purposes. Income sufficiency and education were used as proxy indicators of socio-economic status (SES).

Statistical analyses

The Analysis of de-identified data was conducted using SPSS IBM Statistics version 22 and STATA version 13. Descriptive analysis was used to explore the distribution of participants by selected demographic characteristics and CVDRF. Counts and percentages among the total sample and by dementia diagnosis were produced for categorical variables while means and

standard deviations were calculated for continuous ones. Factors associated with dementia at the bivariate level (p-value < 0.2) were considered for multivariable analysis. A generalized estimating equation (GEE) logistic model was used to account for cluster effect (Galbraith et al., 2010). Unadjusted and adjusted odds ratios (OR) with their 95% confidence intervals (CI) were reported in addition to indication towards p-values less than 0.01 and 0.05.

Results

The mean age of respondents was 72.4 ± 7.2 years and there were slightly more females (56.2%) than males. The majority had a living spouse (62%) and almost 80% have had a formal education in their life. Close to one third of participants perceived their personal income as insufficient. Around one third were ever smokers (35.1%) and one fourth current smokers (24.3 %) with higher proportions among males as compared to females (ever smokers: 47.0% vs. 25.9%; current smokers: 33.7% vs. 17.1%). Less than one in seven older adults (13.4%) reported ever drinking alcohol. While the majority perceived themselves as fairly or very physically active (84.7%), around 55% of older adults were overweight and 27% were obese. More than half of the participants reported having hypertension (52.3%) with significantly higher proportions among females (57.1%) as compared to males (46.0%). The majority of hypertensive participants were classified as having "uncontrolled" hypertension (60.4%). Diabetes was reported by 32% of the participants, while heart problems were reported by almost one fifth of the sample. A total of 37 older adults (7.4%) were diagnosed with dementia using the 10/66 algorithm.

Table 1 summarizes the crude and adjusted estimated effect measures of demographic, behavioral and health related factors with the outcome dementia. The proportion of older adults with dementia significantly increased with higher age categories, reaching 20.6% for those aged 85 years; the odds of dementia was also significantly higher among females, those who were currently unmarried, those with no formal education, and those reporting insufficient income. As for CVDRF, lower pack-years of cigarette smoking, not being physically active, having heart problems, and being hypertensive and/or diabetic (p-values were statistically significantly associated with higher probability of having dementia.

All variables, except for BMI and alcohol consumption, had a p-value for unadjusted associations lower than 0.2 and were thus included in the multivariable analysis. Results of the adjusted odds ratios show that higher age group, perception of personal income as insufficient (p-values < 0.01), and uncontrolled hypertension (p-value < 0.05) remained strongly and positively associated with having dementia. Female gender increased the odds of having dementia by at least two times when controlling for all other factors yet the result was not statistically significant.

[TABLE 1 HERE]

Discussion

Similar to other findings in the literature, our study revealed that demographic and socio-economic characteristics of the older adult and CVDRF, namely older age, insufficient income, and uncontrolled hypertension, are important factors associated with dementia in the Lebanese context. Advanced age is a well-established risk factor for dementia, yet some evidence shows that the disease incidence stabilizes after the age of 84 (Gao et al., 1998). In our study, less than 7% of older adults were in the age group 85+ years, thus cases were aggregated preventing the visualization of any trend in dementia prevalence at the end of this age spectrum. Our analysis showed that female gender was strongly related to dementia but only at the bivariate level. In the published literature the association between female gender and dementia is still inconclusive (Arslantas et al., 2009; Ertekin et al., 2015).

The association between low SES and dementia is well established in the literature. Studies reported that a positive correlation exists even in a homogeneous population of socially-disadvantaged individuals (Keskinoglu et al., 2006; Yaffe et al., 2013; Zeki Al Hazzouri et al., 2011). In parallel, our results showed a strong and positive association between income sufficiency and dementia, controlling for other factors including education. Researchers have attributed this association to poor access to health care services, unhealthy diet or lifestyle, low education, and increased physiological stress that can contribute to higher blood pressure and depression (Camacho-Mercado et al., 2016; Yaffe et al., 2013). While some studies on dementia used income level and occupation as proxies for SES (Keskinoglu et al., 2006), others have selected “self-perceived SES” or “financial adequacy” (Keskinoglu et al., 2006; Yaffe et al.,

2013). The latter measure on income sufficiency constitutes a subjective indicator that is strongly related to main socio-economic characteristics of the household and depends positively on absolute family income (Gori-Maia, 2013). In our data, the most adequate income measure to be used as a proxy for SES was income sufficiency.

Comparable to other studies (Warchol-Celinska et al., 2015), our results showed that uncontrolled hypertension increased the odds of dementia while adjusting for other socio-economic and CVDRF. Additional evidence from the preDIVA RCT, a 6-year multi-domain vascular care intervention, further emphasized the role of treating high blood pressure among the uncontrolled group in reducing the risk of dementia (Moll van Charante et al., 2016). Yet, the biological mechanisms explaining this association are not well understood. Some studies showed that a poorly controlled blood pressure is associated with a decline in cerebral blood flow, an increase in white matter hyper-intensity volume, lacunar infarcts and cerebral micro-bleeds (Hughes and Sink, 2016; Poels et al., 2012). This factor is of particular importance in the Lebanese context since close to one fourth of adults above 30 years of age are hypertensive (Tohme et al., 2005), with higher estimates for those aged 60 years and above (58.4% for females and 44.0% for males) (Sibai et al., 2009). The latter figures are comparable to the ones from our study. A more salient result is the high burden of uncontrolled hypertension detected in our study (31.6%), a common finding among older adults residing in developing countries, with rates expected to increase as a result of the ongoing health transitions (Prince et al., 2012).

Overall, there is an increasing body of evidence pointing to the importance of midlife CVDRF as predictors of dementia and/or its subtypes, yet mainly based on observational research (Suemoto, 2015). A recently published study from the USA based on two cohorts revealed a decreasing trend in dementia prevalence between 2000 and 2012 which was attributed to better treatment of CVDRF (Langa et al., 2017). However, meta-analyses of available randomized controlled trials failed to show a dementia risk reduction associated with treatment of diabetes, hyperlipidemia or hypertension, possibly due to methodological limitations in the design of these trials such as short duration of follow up and treatment initiation at advanced ages (above 50 years) (Suemoto, 2015).

Strengths and Limitations

The diagnosis of dementia was based on validated tools with good psychometric properties (Phung et al., 2014), which enhances the internal validity of the study in terms of accurate case detection. The multi-stage cluster sampling with number of participants proportionate to the respective populations residing in Beirut, Chouf and Aley made the study sample representative of these selected areas thus enhancing the external validity of the study. Moreover, Analysis was conducted taking into account the clustering effect which led to robust results.

Having adopted a cross-sectional study design, the temporal relationship between risk factors and outcome cannot be determined. Yet, other studies examined associations between similar exposures and dementia using a cohort design and found comparable results (Suemoto, 2015; Whitmer et al., 2005; Yaffe et al., 2013). With the exception of measured blood pressure, all the information collected were self-reported which potentially might lead to recall bias, more likely to be a non-differential bias.

Conclusion

This is the first study in Lebanon that examines dementia risk factors. It highlights the importance of SES and CVDRF, namely uncontrolled blood pressure, in the etiology of dementia. The findings are applicable to other upper-middle income countries in the region (Jordan, Turkey, Cyprus, Greece, Oman, and others) that share similar socio-demographic characteristics, cultural, and lifestyle factors and whose disease burden due to cardiovascular diseases and their risk factors is equally high.

Multi-domain clinical trials addressing diet, exercise, cognitive training and vascular risk monitoring have documented an improvement of cognitive functioning (Ngandu et al., 2015). These types of interventions are difficult to do on a large scale and could be implemented with persons who are at high risk of cognitive decline or dementia such as low SES/disadvantaged adults. Interventions targeting specifically patients with uncontrolled hypertension are recommended and should be tailored to the context and health care system of the country. Such interventions mainly include self-monitoring of blood pressure, patient education, health professional (nurse, pharmacist, and general practitioner) education, reminder systems, and

regular review and follow up of hypertensive patients within an organized system of healthcare delivery (Fahey et al., 2005; Glynn et al., 2010).

A major contributor to poor blood pressure control is lack of adherence to medication which could have resulted from complex drug regimens, long duration of therapy, medication side effects, lack of disease symptoms, and/or poor patient understanding of hypertension management among others (Schroeder et al., 2004). The most effective intervention toward increasing medication adherence is the prescription of simple dosing regimens followed by providing patient motivation through reminders and family-member support as examples (Schroeder et al., 2004). These strategies, if implemented at the ambulatory care and home care levels, could contribute to improved patient compliance and potentially better control of blood pressure.

Moreover, efforts should be made to increase awareness among people of young or middle age groups on the benefits of leading a healthy lifestyle to prevent hypertension, or have an early diagnosis of hypertension among other CVDRF. As for the older adult, it is recommended that the physician adopts a holistic approach when examining or following up on the patient through screening for CVD such as hypertension, diabetes and stroke. This will contribute to early detection or treatment decreasing the burden of CVD as well as cognitive decline.

Finally, interventions and policies that could target risk factors for low SES include: improving access to health care through decentralization of services, strengthening the public health sector, working towards achieving a universal health coverage, and offering support for access to primary health care services such as screening for chronic diseases to those with low or insufficient income. Yet research that investigates the effectiveness of such interventions in lowering the risk of dementia are needed to better understand the role of low socio-economic status in the development of the disease.

Conflicts of interest

None.

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Table 1: Association between dementia and socio-demographic and cardiovascular disease risk factors. Lebanon, 2013 (N = 502).

Covariates		Total N (%)	Dementia n (%)	unOR (95% CI)	adjOR (95% CI)
Socio-demographics					
Age (years)	64 - 74	330 (65.7)	13 (3.9)	1.0	1.0
	75 - 84	138 (27.5)	17 (12.3)	3.38** (1.59; 7.16)	4.00** (1.46; 10.95)
	85 +	34 (6.8)	7 (20.6)	6.21** (2.30; 16.78)	7.07** (1.84; 27.03)
Gender	Male	220 (43.8)	6 (2.7)	1.0	1.0
	Female	282 (56.2)	31 (11.0)	4.25** (1.76; 10.26)	2.40 (0.73; 7.91)
Marital status	Married	304 (62.0)	11 (3.6)	1.0	1.0
	Unmarried	186 (38.0)	23 (12.4)	3.70** (1.77; 7.74)	1.03 (0.39; 2.68)
Education	Formal	401 (79.9)	21 (5.2)	1.0	1.0
	Not formal	101 (20.1)	16 (15.8)	3.39** (1.71; 6.70)	1.28 (0.52; 3.13)
Income	Sufficient	356 (73.3)	16 (4.5)	1.0	1.0
	Insufficient	130 (26.7)	17 (13.1)	3.27** (1.61; 6.67)	3.90** (1.58; 9.60)
CVD risk factors					
Body Mass index	Normal	87 (17.8)	7 (8.0)	1.0	
	Overweight	269 (55.1)	16 (5.9)	0.72 (0.28; 1.81)	
	Obese	132 (27.0)	12 (9.1)	1.14 (0.43; 3.02)	
Cigarette smoking (pack-years)	N	461	31	0.97*	0.97
	(Mean ± SD)	(13.9±26.5)	(4.1±11.5)	(0.94; 0.99)	(0.94; 1.00)
Alcohol consumption	No	421 (86.6)	31 (7.4)	1.0	
	Yes	65 (13.4)	2 (3.1)	0.39 (0.09; 1.67)	
Physical activity	Yes	415 (84.7)	24 (5.8)	1.0	1.0
	No	75 (15.3)	10 (13.3)	2.47* (1.13; 5.41)	1.77 (0.67; 4.66)
Hypertension	No	233 (47.7)	5 (2.1)	1.0	1.0
	Controlled	101 (20.7)	9 (8.9)	4.41** (1.45; 13.41)	2.46 (0.56; 10.85)
	Uncontrolled	154 (31.6)	20 (13.0)	6.66** (2.46; 17.99)	6.35* (1.60; 25.10)
Diabetes	No	334 (68.0)	16 (4.8)	1.0	1.0
	Yes	157 (32.0)	18 (11.5)	2.52** (1.26; 5.04)	1.73 (0.70; 4.23)
Heart problem	No	386 (78.6)	22 (5.7)	1.0	1.0
	Yes	105 (21.4)	12 (11.4)	2.09* (1.00; 4.38)	1.35 (0.55; 3.34)

Abbreviations: adjOR, adjusted odds ratios; CI, confidence interval; CVD, cardiovascular disease; N, n, number; SD, standard deviation; unOR, unadjusted odds ratios.

* P-value < 0.05; ** P-value <0.01.

Highlights:

- This is the first community-based dementia prevalence study conducted in Lebanon.
- Monitoring adherence to hypertension medication is a needed dementia intervention.
- The association between dementia and socio-economic status warrants more research.