Original Article

Association between multimorbidity and cognitive decline in the elderly population of the Eastern Province, Saudi Arabia

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Abstract:

BACKGROUND: Cognitive decline affects the quality of life, and dementia affects independence in daily life activities. Multimorbidity in older adults is associated with a higher risk of cognitive impairment. This research aims to study the relationship between cognitive decline and multimorbidity in the elderly population in the Eastern Province, Saudi Arabia.

MATERIALS AND METHODS: This cross-sectional research was conducted from July to October 2022 among adults over 60 years. All patients with two or more comorbidities were contacted for a face-to-face interview and cognitive testing to estimate cognitive function by trained family physicians using St. Louis University Mental State Examination. ANOVA and Chi-square test were used to test for statistical significance. Binary logistic regression was used to show the odds of having cognitive impairment and multimorbidity. All tests were performed at 5% level of significance.

RESULTS: The study involved 343 individuals; majority (74.1%) aged 60-75 years and were males (67.9%). Hypertension, diabetes, and chronic pain were reported by 56%, 48%, and 44% participants, respectively. Thirty percent participants had 3 or more comorbidities. About 36% had mild neurocognitive disorder and 31.2% had dementia. The results showed that age, gender (female), diabetes, stroke, chronic pain, and multimorbidity were significantly associated with cognitive impairment. In our study, hypertension, coronary artery diseases, depression, and anxiety were not significantly associated with risk of cognitive decline.

CONCLUSION: Our study found that multimorbidity is significantly associated with cognitive decline. Controlling comorbidities and preventing risk factors in midlife could help in delaying the progression of the disease.

Keywords:

Chronic diseases, dementia, mild cognitive impairment, multimorbidity

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Introduction

Dementia is defined by the diagnostic and statistical manual of mental disorders fifth edition as decline in one or more of the cognitive domains in comparison to the previous norm of the person that affects the independence of performing daily life activities.[1]

More than 55 million people in the world live with dementia as per the World Health Organization.[2] Data on the prevalence of dementia and cognitive impairment in Saudi Arabia are scant; one study found that the prevalence of dementia was

6.4% in Saudi Arabia and that the prevalence of mild cognitive impairment (MCI) was 38.6% in the geriatric population.[3] Another study found the prevalence of dementia as between 11% and 16%.[4]

Worldwide, a report on Alzheimer's disease indicated that there were 46.8 million people with dementia in 2015 and estimated that the number would rise to 74.7 million and 131.5 million in 2030 and 2050, respectively.[5] However, a newer study states that the approximate number of people with dementia is 57 million and estimates that this number would rise to more than 152.8 million in 2050.[6]

Fortunately, in the last 20 years, there has been a reduction in the age-adjusted incidence, which is most likely because of awareness and education; however, the impact and sequence of dementia are still significant.[7] Locally, the estimated prevalence of dementia in Saudi Arabia is between 11% and 16%.[4]

The most recognized risk factor for dementia is aging, and that is supported by many epidemiological studies. Alzheimer's disease facts and figures (2020) indicate that Alzheimer's disease affects 5%–10% of people who are older than 65 years and 50% of those who are older than 85 years.[8] Risk factors are usually classified as modifiable or nonmodifiable. Modifiable risk factors include diet, restricted physical activity, lack of social activities, smoking, and alcohol consumption. Other modifiable risk factors are preventable chronic diseases such as diabetes, hypertension, chronic pain, stroke, and ischemic heart diseases. Psychological stress in the form of depression, anxiety, and delirium was shown in the literature to affect the cognitive function.[9,10] The nonmodifiable risk factors include being female, black race, and genetic factors like the apolipoprotein E gene.[11,12]

Dementia and MCI are two different stages of the same disease. Dementia is when the patient is unable to perform one or more of the activities of daily living (ADL). A broader term of description for both is "cognitive decline."[13] These are crucial topics to discuss because they have a significant impact on the patient's quality of life. Cognitive decline negatively influences self-care and self-management of other chronic diseases and decreases engagement in health-enhancing activities.[14] Furthermore, it causes certain changes in the patient's personality, leading to difficulties in their lives and that of their families.[1]

Another aging-related phenomenon is multimorbidity, which can be defined as having at least two chronic diseases simultaneously.[15,16] Multimorbidity was found to increase the risk of hospital admission, a longer length of stay, and premature death.[17] A systematic review in 2019 estimated that 33.1% of people of any age, and approximately 50% of people who are older than 65 years, have multimorbidity.[18] In Saudi Arabia, approximately 23.3% have multimorbidity.[19]

These two common aging-related phenomena are being thoroughly studied around the world and have been shown to influence each other negatively, resulting in synergetic poor outcomes.[13,20] Furthermore, it has been found that patients who have multimorbidity are very likely to have dementia, with the risk increasing significantly when there are 3 or more chronic diseases, and the onset of multimorbidity is before the age of 55 years.[15] This situation is challenging for providers of primary and secondary healthcare because some conditions tend to exacerbate dementia progression.[13] On the other hand, patients who have dementia need a special approach for other comorbid diseases they have, such as diabetes or hypertension.[13]

As stated in the Health Sector Transformation Program report (2021), Saudi Arabia is focusing on enhancing health generally to increase life expectancy specifically as part of the 2030 vision.[21] Life expectancy in Saudi Arabia was 45 years in 1960, but has increased by 30 years to the current 75 years approximately.[22] This change is likely to lead to an increase in age-related illnesses, which underlines the importance of studying dementia and multimorbidity thoroughly. Moreover, a study of the risk factors of dementia will help eliminate them or get them under control, which in turn would hopefully lead to a healthy elderly population with high quality of life. This research aims to study the relationship between cognitive decline and multimorbidity in the elderly population in the Eastern Province of Saudi Arabia.

Materials and Methods

This was a cross-sectional study conducted from July to October 2022. Participants were chosen from the COVID-19 vaccination center and outpatient clinics in Dammam city, Saudi Arabia. Our inclusion criteria were individuals aged 60 years or older as per the Saudi Ministry of Health rule for the definition of the elderly. Excluded from the study were any that had experienced any head trauma in the previous 3 months. Ethical approval was obtained from the Institutional Review Board (IRB Number-2022-01-136) dated 27/03/2022, and written informed consent was taken from all participants in the study. The written consent clearly indicated that participation in this study was voluntary and that all data would remain confidential.

The variables assessed in the study were the following: any chronic disease the participant may have,

participant's age and gender, and their dementia diagnosis (normal: scoring 25–30; mild neurocognitive disorder: scoring 20–24; or dementia: scoring 1–19). Surveys were completed using face-to-face interviews by geriatricians or physicians trained by geriatricians to conduct the interview. The survey collected data on participants' sociodemographic variables and medical history, including diabetes mellitus, hypertension, and coronary artery diseases. Information about stroke, depression, anxiety, and multimorbidities were collected as well. Our definition for multimorbidities was more than one chronic disease other than dementia, of the above-mentioned chronic diseases in a patient. A validated Arabic version of St. Louis University Mental Status (SLUMS) examination was used.[23]

The SLUMS is a 30-point, 11-item scale that is used to identify people with dementia or MCI. The total possible score is 30. Scores interpretation depends on the educational level; high school education: normal: 27–30; MCI: 21–26; dementia: 1–20. Less than high school education: Normal: 25–30; MCI: 20–24; dementia: 1–19. A validated Arabic version of the SLUMS was used in our study, as it was easier for our population to understand, and our diagnosis of dementia and MCI were based on it.[23]

Considering 34.5% prevalence of multimorbidity in older adults in Saudi Arabia,[24] precision of 5%, and 5% significance level, the calculated sample size using Epi Info 7.0[25] was 343. A systematic sampling technique was used, picking every fourth listed patient and six research assistants approached the selected participants. All patients with two or more comorbidities were contacted for a face-to-face interview and cognitive testing by trained family physicians using SLUMS.[23]

For the data analysis, frequencies and percentages were calculated to show the summaries of the study variables. In addition, Kruskal–Wallis H test was used for nonparametric analysis in the study, while ANOVA and Chi-square test were used for the rest of the analysis. In addition, binary logistic regression was used to show the odds of having cognitive impairment and having multimorbidity. All statistical tests were two-sided, using $P = 0.05$ for statistical significance. Analyses were performed using Statistical Package for the Social Science (SPSS) version 27 (IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp., USA).[26]

Results

There were 343 study participants with an average age of 65 years. More than 65% of them were males. Almost half of the participants stated that they had diabetes

and 56% had hypertension. The majority indicated that they never had a coronary artery disease (82%) or stroke (92%).

Regarding mental well-being, only 2% indicated that they had depression and only 7% had anxiety. In addition, 44% of the participants indicated that they had chronic pain. The average number of chronic diseases for each participant in the study was 1.8 [Table 1].

Age and gender were significantly related to the participant being diagnosed with dementia (Kruskal–Wallis H = 9.92, $P = 0.007$; and $\chi^2 = 9.06$, $P = 0.011$, respectively). Participants who had dementia were significantly older and were more likely to be females than those without dementia as shown in Table 2.

Some of the chronic diseases assessed in the study showed a significant association with dementia. The results showed that diabetes was significantly associated with dementia ($\chi^2 = 11.214$, $P = 0.004$) as most diabetic patients in the sample had dementia (40% of all diabetic patients). In addition, stroke was another important disease that is significantly associated with dementia ($\chi^2 = 11.789$, $P = 0.003$) as 58% of all participants with stroke had dementia, while only 8% of patients who had a history of stroke did not have neurocognitive disorder, i.e. no dementia symptoms.

Table 1: Characteristics of elderly persons in Dammam city, Saudi Arabia, 2022 (*n*=343)

Variables	*N* (%)
Age (years old)	
60–75	254 (74.1)
75–90	75 (21.9)
Missing	2 (0.6)
Gender	
Male	233 (67.9)
Female	110 (32.1)
Chronic diseases	
Diabetes	164 (48.0)
Hypertension	191 (56.0)
Coronary artery diseases	63 (18.0)
Stroke	26 (8.0)
Depression	8 (2.0)
Anxiety	25 (7.0)
Chronic pain	151 (44.0)
Chronic diseases (multimorbidity)	
No diseases	60 (17.5)
1–2 chronic diseases	181 (52.8)
3–4 chronic diseases	94 (27.4)
5–7 chronic diseases	8 (2.3)
Average chronic diseases	
Mean±SD	1.8±1.3
Median (IQR)	2 (2)

SD=Standard deviation, IQR=Interquartile range

Table 2: Cognitive impairment among elderly persons by demographics and comorbidities, Dammam city, Saudi Arabia, 2022 (*n*=343)

Variables	Dementia Assessment SLUMS categories			P-value
	Normal (*n*=113) N (%)	Mild neurocognitive disorder (*n*=123) N (%)	Dementia (*n*=107) N (%)	
Age				0.040
60–75 years old	109 (96.5)	115 (93.5)	92 (87.6)	
76–90 years old	4 (3.5)	8 (6.5)	13 (12.4)	
Gender				0.011
Male	85 (75.2)	87 (70.7)	61 (57.0)	
Female	28 (24.8)	36 (29.3)	46 (43.0)	
Diabetes				0.004
No	69 (61.1)	68 (55.3)	42 (39.3)	
Yes	44 (38.9)	55 (44.7)	65 (60.7)	
Hypertension				0.074
No	48 (42.5)	64 (52.0)	40 (37.4)	
Yes	65 (57.5)	59 (48.0)	67 (62.6)	
Coronary artery diseases				0.154
No	98 (86.7)	100 (81.3)	82 (76.6)	
Yes	15 (13.3)	23 (18.7)	25 (23.4)	
Stroke				0.003
No	111 (98.2)	114 (92.7)	92 (86.0)	
Yes	2 (1.8)	9 (7.3)	15 (14.0)	
Depression				0.355
No	109 (96.5)	112 (99.2)	104 (97.2)	
Yes	4 (3.5)	1 (0.8)	3 (2.8)	
Anxiety				0.846
No	106 (93.8)	113 (91.9)	99 (92.5)	
Yes	7 (6.2)	10 (8.1)	8 (7.5)	
Chronic pains				0.034
No	74 (65.5)	66 (53.7)	52 (48.6)	
Yes	39 (34.5)	57 (46.3)	55 (51.4)	
Chronic diseases				<0.001
Mean±SD	1.6 (1.2)	1.7 (1.3)	2.2 (1.4)	

SD=Standard deviation, SLUMS=St. Louis University Mental State Examination

Using the SLUMS Scale, most participants who indicated that they had chronic pain were diagnosed with mild neurological disorder (38% of all patients with chronic pain), followed by dementia (36% of all patients with chronic pain), and the association between having chronic pain and dementia was statistically significant (χ^2 = 6.78, P = 0.034).

Furthermore, the increased number of chronic diseases in the same participant had a significant effect on their dementia diagnosis (f = 7.60, P < 0.001); patients with more chronic diseases were more prone to have dementia. In this study sample, individuals who were diagnosed with dementia using SLUMS scale had 2.2 chronic diseases [Table 2].

Several chronic diseases in the study did not show any significant association with dementia. These included hypertension (χ^2 = 5.207, P = 0.074), coronary artery diseases (χ^2 = 3.746, P = 0.154), depression (χ^2 = 2.07, P = 0.355), and anxiety (χ^2 = 0.34, P = 0.846).

Table 3 shows the crude and adjusted odds ratios for having cognitive impairment and its influencing variables. While at the crude level of logistic regression, all the variables that were significant at the bivariate analysis were significantly related to having cognitive impairment except chronic pain. However, after adjusting the model for all the significant variables at the bivariate level of analysis, only gender and diabetes remained significantly related to having cognitive impairment. The odds of having cognitive impairment were two times higher in females than in males, as well as two times higher in patients with diabetes compared to those without diabetes.

Discussion

Two-thirds of our sample of 343 elderly participants had cognitive decline. However, this study could be overestimating the prevalence of cognitive decline, as most of the participants who came to the outpatient clinics or vaccination center had chronic diseases;

Table 3: Binary logistic regression analysis: Association between cognitive impairment and having multicomorbidity among elderly person, Dammam city, Saudi Arabia, 2022 (*n*=343)

Variables	Crude OR	*P*-value	95% CI	Adj. OR	*P*-value	95% CI
Age (years old)						
60–75	1.0		-	1.0		-
76–90	2.64	0.021	1.16–6.00	2.40	0.052	0.99–5.81
Gender						
Male	1.0		-	1.0		-
Female	2.03	0.004	1.26–3.27	2.03	0.006	1.22–3.36
Diabetes						
No	1.0		-	1.0		-
Yes	2.14	0.001	1.34–3.41	1.97	0.041	1.03–3.74
Stroke						
No	1.0		-	1.0		-
Yes	3.34	0.004	1.48–7.53	2.76	0.054	0.98–7.76
Chronic pain						
No	1.0		-	1.0		-
Yes	1.54	0.065	0.97–2.44	1.21	0.557	0.64–2.32
Chronic diseases (multimorbidity), mean±SD	1.38	<0.001	1.16–1.65	1.02	0.897	0.73–1.43

Binary logistic regression model: Nagelkerke R^2=0.120, *P*<0.001. CI=Confidence interval, Adj.=Adjusted, OR=Odds ratio, SD=Standard deviation

therefore, there may be a selection bias in this study. Moreover, ADLs were not studied in our research.

Our findings suggested that the nonmodifiable risk factors of cognitive impairment are being female and old age. The modifiable risk factors that were significantly associated with dementia are diabetes, history of stroke, chronic pain, and multimorbidity. Coronary artery diseases, depression, and anxiety were not significantly associated with dementia in our study. However, only 2% of our sample had depression and 7% had anxiety. In addition, hypertension was not significantly associated with dementia in our study; however, this can be attributed to the lack of detail about the level of control of hypertension in our participants.

In our country, there is a dearth of studies on dementia and its risk factors. Existing studies in literature showed conflicting results. A cross-sectional research done in Riyadh, Saudi Arabia, on the risk factors of dementia in geriatric patients attending primary healthcare centers, found that depression was the most significant modifiable risk factor.[4] In contrast, our study could not assess the association between depression and cognitive decline owing to the lack of participants with depression.

Another research done in Riyadh, Saudi Arabia, concluded that age, hypertension, and cardiovascular disease were the main risk factors of cognitive impairment.[3] However, the sample size of that study was 171; therefore, we could not reliably comment on those results. Hypertension and coronary artery disease were not risk factors for dementia in our study population.

Globally, almost all published research papers stated that multimorbidity had a significant negative impact on a patient's cognitive function and increased the risk of developing dementia. Current literature agrees that multimorbidity will have a negative impact on the development of dementia, while there is no consensus on how significantly each disease is related to dementia. These risk factors differ between different countries and races.

A systematic review and meta-analysis published in 2019 to study the impact of having more than one risk factor on developing cognitive impairment found that having more than one risk factor will negatively affect cognitive function.[9] A population-based prospective cohort study published in 2022 on 206,960 participants on the impact of multimorbidity on developing dementia in people with and without genetic risk for dementia found that multimorbidity was a significant risk factor for developing dementia.[27] However, the researchers concluded that the risk differed with each disease cluster, between male and female and between people with different genetic risks.

Diabetes is positively associated with having dementia. Approximately 40% of the diabetic participants in our study had dementia, and the relationship between diabetes and dementia was statistically significant. This was also noticed in some population-based studies which support our findings.[28,29] Meta-analyses that studied the association between diabetes mellitus and dementia reported a risk ratio of 1.43–1.62.[30-34] The clear pathophysiology is still under study and yet to be discovered in detail, but one of the many hypotheses is that the vascular changes that occur with diabetes mellitus lead to accelerated brain aging and cognitive impairment in diabetic elderly compared to the nondiabetics.[35]

Stroke is a well-known risk factor for dementia worldwide. This was proven by a meta-analysis of 48 international studies conducted in 2018.[36] Our result is consistent with the literature; strokes were positively associated with dementia among our participants. However, only 26 participants (8%) had had a stroke. Further, 58% of those participants who had a previous history of stroke developed dementia, 8% did not have any form of cognitive dysfunction, and the remainder had mild neurocognitive impairment.

Hypertension has been considered a risk factor for cognitive dysfunction. Multiple studies in the literature concluded that hypertension, especially untreated hypertension diagnosed in the 4th and 5th decades of life, was a risk factor for cognitive impairment. The pathophysiology behind this relationship is believed to be caused by cerebral vascular changes that lead to decreased brain perfusion.

These changes depend on the time of diagnosis and control of blood pressure.[37] This was supported by a meta-analysis of 209 prospective studies that concluded that mid-life, uncontrolled hypertension is significantly related to cognitive decline and dementia.[38] In our study, most of our participants had been diagnosed with hypertension (56%); cognitive decline was higher among those with hypertension, though no significant association between hypertension and dementia was found ($P = 0.07$). However, this can be attributed to the lack of detail about the level of control of hypertension in our participants.

Heart diseases have been considered a risk factor for dementia in many studies in literature. Heart diseases are believed to affect the brain by decreasing the blood transfusion to the brain.[39] In our study, we studied the relationship between coronary artery diseases and dementia, and no significant relationship was found between them, likely secondary to fewer participants with coronary artery disease. More studies are needed to find the relationship between subtypes of heart diseases and dementia.

Very little evidence was found in the literature regarding the association between chronic pain and dementia. A systematic review published in 2020 stated that there was a significant relationship between certain chronic pain conditions such as migraine and osteoarthritis and dementia.[40] In our study, the association between chronic pain and dementia was statistically significant. However, more studies are needed to find the relationship between certain pain conditions and dementia subtypes.

Multimorbidity was clearly associated with dementia in the literature, and this is consistent with our results.[27]

However, the literature revealed a debate on which diseases were more significantly associated with later development of dementia. There is a dearth of studies on dementia and its associated risk factors in Saudi Arabia, even though dementia is a serious health condition, the prevalence of which is expected to increase because of the growing population.

The possibility of preventing dementia remains a matter of debate as multiple pathophysiological pathways are involved. Many studies in the literature support the position that many dementia cases can be prevented by controlling its risk factors from the early stages of life.[41] Other studies have stated that dementia can only be delayed by controlling the modifiable risk factors as some risk factors are nonmodifiable.[42] However, both prevention and delay will enhance the quality of life and should be taken into account. This research emphasizes the importance of controlling risk factors of cognitive impairment, especially chronic diseases, as stated above. These risk factors should be controlled from the early stages of life to delay the onset of cognitive impairment in the elderly population. More research is needed to establish the causative relationship between each modifiable risk factor and cognitive impairment. Such research should be done in Saudi Arabia as the literature supports the genetic role in the development of cognitive impairment and as definition of diseases can vary between different areas.

Some limitations are noteworthy in our study. This was a cross-sectional study that could not establish causation. This study did not address the time of diagnosis or the level of control of each chronic disease; neither did it differentiate between different types of dementia and their relation to these risk factors. The questionnaire did not elicit any information on family history of dementia since heredity plays an important role in the development of the disease. Causation cannot be assumed in cross-sectional studies, only the association between risk factors and the disease can. Moreover, it is subject to recall bias since the information given was self-reported.

Conclusion

Our research study found that multimorbidity is associated with cognitive decline. Further, modifiable risk factors that were significantly associated with cognitive decline are diabetes, history of stroke, and chronic pain. This issue is crucial as the life expectancy in Saudi Arabia rises and dementia, an age-related disease significantly affects the ADL. Controlling comorbidities and preventing risk factors in midlife could help in delaying the progression of the disease.

Prospective cohort studies are recommended to establish causative relationships between these modifiable risk factors and cognitive impairment. Addressing the level of control of each risk factor and the time of diagnosis as well as subdividing dementia to its subtypes would help provide a better understanding of how to prevent or delay dementia and MCI and would help in the generalization of the results.

Conflicts of interest
There are no conflicts of interest.

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