Neurocognitive dysfunction among type 2 diabetes patients attending primary health care in Jeddah, Saudi Arabia

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ABSTRACT

Context: Identification of modifiable risk factors of neurocognitive dysfunction (NCDs) that would help in preventing neurocognitive dysfunction by means of appropriate measures. **Objectives:** The study aims to provide an insight into the extent and cofactors of NCDs among Saudi type II diabetes (T2DM) patients at the primary care level. **Settings and Design:** A cross-sectional study was conducted at five randomly selected primary health care centers (PHCCs) of Jeddah, Saudi Arabia. **Subject and Methods:** T2DM patients above 40 years, who were followed for T2DM diagnosed ≥ 1 year ago were recruited. The Arabic version of the Mini-Mental State Evaluation (MMSE) was used for screening NCDs, using education-adjusted cut-offs. **Statistical Analysis Used:** Sociodemographic, diabetes-related, and other clinical and lifestyle factors were analyzed as cofactors of NCDs. **Results:** The study included 236 T2DM patients, who had mean ± SD age of 60.29 ± 9.45 years. The majority (61.0%) were female, and mean ± SD duration of T2DM was 14.1 ± 8.4 years (range = 1–45 years). The prevalence of NCDs was 35.2% (95% CI = 29.1%, 41.6%), and 5.1% of the participants had MMSE scores ≤ 10 indicating severe neurocognitive impairment. The congruence of significant sociodemographic factors delineated a high-risk profile, and multivariate regression analysis showed female gender, low educational level, longer duration of diabetes, geriatric age at T2DM diagnosis, inadequate glycemic control, and sedentary lifestyle as the independent risk factors for NCDs. **Conclusions:** The population of middle-aged and older T2DM patients is highly exposed to NCDs, with the great contribution of other comorbidities and higher risk incurred by older, lowly educated females with long diabetes duration. Further improvements should be achieved to enhance the care offered to diabetic patients by improving glycemic control, screening for comorbidities, and early detection of neurocognitive decline.

Keywords: Cofactors, neurocognitive dysfunction, Saudi Arabia, type II diabetes

Introduction

Local data about the prevalence and epidemiological determinants of NCDs among the diabetic population is scarce despite high local figures and increasing incidence of diabetes. Identifying modifiable risk factors of NCDs may contribute to the prevention by means of appropriate measures. Therefore, the present study aims to provide an insight into the extent of cognitive decline among Saudi type II diabetes patients at the primary care level, by estimating the prevalence of NCDs in a representative sample of diabetic patients. Further, it explored the cofactors of NCDs and identified the modifiable risk factors, which will provide valuable indications on awareness and prevention.

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Theoretical background

Neurocognitive dysfunction (NCD) is not a well-known complication of type 2 diabetes mellitus (T2DM) unlike other complications, rarely screened in clinical practice. There is a highly suspected causal relationship between diabetes and impairment of neurocognitive functions.[1] Epidemiological figures estimate the relative risk (RR) for developing any type of dementia (~1.65 to ~2.5), Alzheimer's disease (~1.41 to ~1.73), and vascular dementia (~1.94 to ~2.66) among T2DM patients as compared to nondiabetic individuals.[2-4] Furthermore, the subtle decline in neurocognitive performance, notably in learning, memory, and executive functions is often detected in T2DM patients without dementia. However, type 1 diabetes patients are associated with structural changes in brain imaging.[4-7]

The major mechanism underlying the impairment of NCDs in diabetes highlights the vascular damage of the brain arterial network resulting from diabetes-induced dysmetabolic and inflammatory changes of the central nervous system.[8,9] Uncontrolled diabetes, indicated by either elevated glycated hemoglobin and chronic hyperglycemia, was thoroughly demonstrated to induce a decrease in cognitive performance and to be directly associated with dementia.[10,11] Other complex mechanisms have been highlighted, suggesting bidirectional interaction between T2DM and NCDs, where NCDs contribute to the pathogenicity of diabetes via modifications of central and peripheral insulin signaling, and vice versa. Principally, these mechanisms involve molecular and cellular changes, such as reactive oxygen species, neurotransmitter and synaptic alterations, and death and changes in neurons and astrocytes.[12] Besides these pathophysiological mechanisms, several genetic, epigenetic, environmental, and behavioral factors also play an important role in the development of NCDs in T2DM.[12]

A study was conducted by Alfahadi *et al.*[13] on the diabetic population during fasting. They revealed that in terms of motor performance and working memory capacity, fasting had a substantial impact on tiredness scales and neurocognitive functioning in individuals with T2DM. Fasting, on the other hand, had no effect on the neurocognitive processes examined in healthy people. T2DM had reduced attention flexibility, working memory capacity, and motor performance relative to controls, and the effects were significant during and after fasting.

According to research done in Brazil, even a quick cognitive examination is significant in determining the impact of diabetes on the mental health of this population, which might be relevant to many other low- and middle-income nations. As society ages, the number of older individuals living with diabetes and, perhaps, concomitant cognitive impairment will rise dramatically. As a result, it is anticipated that poor medication adherence and diabetic self-care would provide a significant challenge to future health systems across the world, especially for people with limited resources.[14]

In elderly adults with diabetes, cognitive impairment is a frequent consequence, and both index diseases may share a similar pathogenesis route. The global frequency of co-morbid diabetes and dementia is rising, posing serious personal and public health concerns. Diabetes treatment will continue to provide a distinct challenge for health care workers as dementia progresses and behavioral problems emerge.[15] In Saudi Arabia, the prevalence of T2DM among the adult population was estimated to be 21.8%. This percentage is highest in the Middle East and North Africa (MENA) region, representing one of the highest in the world. Thus, diabetes represents one of the major public health issues.[16] Further, early detection and appropriate management of NCDs may improve patient's quality of life and reduce the economic burden.[17]

Subject and Methods

A descriptive and analytical, cross-sectional study was conducted at the Ministry of Health (MoH) primary health care centers (PHCCs) of Jeddah, Saudi Arabia, between January 2019 and August 2020. The study protocol was reviewed and ethically approved by the Directorate of Health Affairs, MoH, Jeddah and the institutional review board. Informed consent was taken from the participants before enrolment.

The study involved T2DM patients of 40 years and above, who were followed at the participating PHCCs for T2DM diagnosed ≥1 year ago. Patients with disabling neurological disease or any mental disease with symptoms impeding the communication or testing interview were excluded. The exclusion criteria were extended to end-stage diseases such as kidney failure on dialysis, end-stage heart failure, terminal phase cancer, severe head trauma in the past 3 years, or patients on tranquilizers, opioid analgesics, or psychotropic drugs.

Jeddah contains 46 PHCCs distributed in 5 advisory sectors: Northern, Southern, Center, Eastern, and Western sectors. A two-stage stratified cluster sampling method was used. In stage one, two PHCCs were randomly selected from each of the five advisory sectors (strata). This gave rise to 10 participating PHCCs (clusters). In stage 2, convenience sampling was used to recruit approximately 22 eligible patients from each center, until the target sample size was reached. A sample size of 267 patients was calculated to detect an unknown proportion of NCD ($P = 0.5$) among Saudi T2DM patients, with a 95% confidence interval, a two-sided precision of +/-0.06, and 80% statistical power.

The Mini-Mental State Evaluation (MMSE) was used for screening NCDs among T2DM patients. It is the most widely used cognitive test, calculated as a score varying from 0 to 30, with higher scores indicating better cognitive performance.[18] The study used Arabic, culturally validated version of MMSE.[19] Initially, the widely used cut-off of <24, i.e., 23 NCD/24 non-NCD, was adopted to define the cases. However, education-adjusted cut-offs proposed by Kochhann

et al.[20] including illiterate (<21), poor education (primary or lower) (<22), middle level educated (<23), and secondary and highly educated (<24) participants was adopted due to high percentage of illiterates among the study population, which was likely to interfere with patients' scores.

A semi-structured questionnaire was administered to all the participants that included three sections:

Basic demographic data such as age, gender, marital status, educational level, and occupation were recorded because several sociodemographic factors have been demonstrated to impact cognitive function and aging.[21]

This section covered medical history relating to other factors and confounders of NCDs comprehensively, in addition to diabetes-related factors. It was subdivided into seven dimensions: diabetes-related factors (disease duration, treatment, self-management, glycemic control level, etc.), lifestyle factors (eating habits, weight and BMI, smoking, sleep quality, etc.), comorbidities (hypertension, stroke, head trauma, sleep apnea, etc.), physical disability (hearing impairment, visual impairment, etc.), psychological health (history of depression, phobia, etc.), other medications, and family neuropsychiatric history (dementia, depression, psychosis, etc.). History factors were selected in accordance with good clinical practice to assess neurocognitive functions.[21,22]

A training phase was carried out for the first 20 participants, where the MMSE was administered by the investigators under the supervision of a psychiatrist with significant experience in cognitive testing.

The data were analyzed using the Statistical Package for Social Sciences (SPSS) version 21.0. Missing data regarding age, gender, educational level, and the number of children, which concerned <3% of the sample were managed using multiple imputation methods. Mean, median, standard deviation, and range were used to describe the numerical data; whereas, frequency and percentage summarized categorical variables. The prevalence of NCDs was calculated as the percentage of the participants who achieved a total MMSE score lower than the cut-off defined with respect to each participant's educational level. Bivariate analyses were carried out to analyze the sociodemographic factors and other cofactors associated with NCDs. Moreover, the Chi-square test, Fisher's exact test, and independent *t*-test were used, as appropriate. Three multivariate binary regression models were carried using positive NCDs detection as the dependent variable, as following:
- Model 1: showed significance in bivariate analyses
- Model 2: showed significance in bivariate analyses by the exclusion of sociodemographic factors
- Model 3: included significant variables from Model 1.

Results are presented as odds ratio with 95% CI. *P* value <0.05 was considered statistically significant.

Table 1: Participants' sociodemographic characteristics (*n*=236)

Parameter	Category	Frequency	Percentage
Center	Al Mahjar	119	50.4
	KAUH Diabetic clinic	36	15.3
	Al Safa	27	11.4
	ADPF	26	11.0
	Other	28	11.9
Gender	Male	92	39.0
	Female	144	61.0
Age (years)	Mean, SD	60.29	9.45
Marital Status	Single	7	3.0
	Married	142	60.2
	Divorced	23	9.7
	Widowed	64	27.1
No. Children	Median, range	5	0, 16
	None	13	5.5
	1-3	51	21.6
	4-6	89	37.7
	7+	83	35.2
Educational Level	Illiterate	93	39.4
	Primary	66	28.0
	Middle school	32	13.6
	Secondary	22	9.3
	University+	23	9.7
Nationality	Saudi	178	75.4
	Non-Saudi	58	24.6
Residency area	Urban	150	67.6
	Rural/Country	72	32.4
Occupation	Employed	23	10.1
	Housewife	124	54.6
	Unemployed	26	11.5
	Retired	54	23.8
Monthly income (SAR)	<5 K	117	53.4
	5 K-10 K	77	35.2
	10 K-15 K	22	10.0
	>15K	3	1.4

Values are frequencies, percentages; except if otherwise specified. For each variable, percentages are calculated on valid answers (by excluding missing values). ADPF: Association of Diabetic Patients Friends; KAUH: King Abdulaziz University Hospital

Results

Sociodemographic characteristics, diabetes-related parameters, and lifestyle, and other clinical parameters are presented in Tables 1-3, respectively. The study included 236 T2DM patients, with a mean (SD) age of 60.3 (9.5) years, and 61.0% of them were female. Of note, the sample included a relatively high percentage of illiterates (39.4%) and low economic class (53.4%) participants [Table 1]. The patients were diagnosed with T2DM at a mean (SD) age of 46.2 (11.1) years, and 71.9% declared regular follow-up with their physician for diabetes since the diagnosis (71.9%). Moreover, 81.4% of them were on oral antidiabetics, and 21.6% of them had uncontrolled diabetes according to their physicians. The prevalence of suspected and confirmed diabetes complications showed retinopathy (20.8% and 6.4%), neuropathy (14.0% and 5.1%), nephropathy (15.7% and 5.5%), and cardiovascular disease (19.9% and 8.9%) [Table 2].

Table 2: Diabetes-related data (*n*=236)			
Parameter	**Category**	**Frequency**	**Percentage**
Diabetes assessment			
Age at diabetes diagnosis (years)	Mean, SD	46.19	11.08
	Range (max., min.)	10	83
	Median, IQR	45	13
Time from diagnosis (years)	Mean, SD	14.10	8.41
	Range (max., min.)	1	45
	Median, IQR	12	12
Do you see the doctor regularly for diabetes?	Yes, since the diagnosis	164	71.9
	Yes, but not since diagnosis	50	21.9
	Yes, just recently	14	6.1
Treatment§	Oral antidiabetic agent	192	81.4
	Insulin	120	50.8
	Diet	35	14.8
Current regimen	OAD alone	95	40.3
	Insulin alone	28	11.9
	OAD + Insulin	68	28.8
	OAD + Insulin + Diet	20	8.5
	Diet alone	2	0.8
	OAD + Diet	9	3.8
	Insulin + Diet	4	1.7
	No treatment	10	4.2
Last capillary glucose measure	Today	75	32.6
	<1 week	78	33.9
	>1 week	71	30.9
	Never	6	2.6
Last measure level	Normal	113	49.1
	Abnormal	73	31.7
	Do not know	44	19.1
Diabetes status	Uncontrolled	51	21.6
	Moderately controlled	114	48.3
	Well controlled	46	19.5
	Do not know	25	10.6
Own a glucometer	No	33	14.8
	Yes	189	84.8
Last HbA1c level (%)	Unavailable	67	28.4
	Available	169	71.6
	Mean, SD	7.49	1.63
Diabetes complications			
Retinopathy	No	172	72.9
	Suspected	49	20.8
	Confirmed	15	6.4
Neuropathy	No	191	80.9
	Suspected	33	14.0
	Confirmed	12	5.1
Nephropathy	No	186	78.8
	Suspected	37	15.7
	Confirmed	13	5.5
Cardiovascular	No	168	71.2
	Suspected	47	19.9
	Confirmed	21	8.9

SD: Standard deviation; IQR: Interquartile range; OAD: Oral antidiabetic agent

Two patients (0.8%) were previously diagnosed with NCDs, both with Alzheimer's disease, and had a history of stroke (5.9%). Three most frequently reported comorbidities were hypertension (64.4%), sleep apnea (23.3%), and coronary artery disease (13.1%). The three most frequent physical disabilities included visual impairment (51.7%), hearing impairment (25.4%), and difficulty walking (23.3%). Psychiatric history showed a high prevalence of anxiodepressive disorder including stress/anxiety (38.1%) and depression (28.0%). Assessment of lifestyle showed the participants with unhealthy eating habits (36.8%), sedentary lifestyle (25.0%), overweight or obesity (49.0%), active smoking (8.3%), and poor sleep quality (24.9%) [Table 3].

The internal consistency of the MMSE was measured by calculating Cronbach's alpha, which was as high as 0.76, indicating its high reliability in the study population. Using standard cut-off, 95 out of the total participants had scores <24, prevalence (95% CI) = 40.3% (33.9%, 46.8%). By using education-adjusted cut-off, the prevalence (95%) of NCDs was 35.2% (29.1%, 41.6%). Of the total participants, 5.1% had scores ≤10 indicating severe neurocognitive impairment.

Participants with NCD were older with a 6-year difference in the mean age from the two groups (*P* = 0.020), as compared with non-NCD ones. Further, the percentage of NCDs was higher among females (41.0% versus 26.1%), widowers (54.7% versus 30.3% or lower), illiterate (54.8% versus 33.3% or lower), rural residents (51.4% versus 28.7%), and unemployed/housewives (42.3% and 41.9% versus 20.4% or lower). All differences were statistically significant (*P* < 0.05) [Table 4].

Regarding diabetes related factors, NCD was associated with T2DM being diagnosed at a relatively older age (~5 years older) compared with non-NCD patients (*P* = 0.001), as well as longer duration of diabetes (>10 years: 44.4% in versus ≤10 years: 24.5%, *P* = 0.001). Similarly, NCDs were more frequent among patients with abnormal result on the last capillary glucose measurement (47.9% versus 25.7%), uncontrolled diabetes (47.4% versus 32.5% or lower), HbA1c ≥7% (45.5% versus 15.8%), and suspected or confirmed cardiovascular complication (51.1% and 47.6% versus 29.2%) [Table 5].

Other clinical cofactors that showed significant associations with NCDs included hypertension (42.1% versus 22.6%), stroke (71.4% versus 32.9%), depression (45.5% versus 31.2%), hearing impairments (56.7% versus 27.8%), visual impairments (42.6% versus 27.2%), speech problems (78.6% versus 32.4%), difficulty walking (52.7% versus 29.8%), and upper limb motor disability (75.0% versus 33.8%). Lifestyle factors that were significantly associated with NCDs included absence of exercise (55.2% versus 20.2% for regular exercise) and nonsmoker status (38.9% versus 15.8% among active smokers) [Table 6].

The three multivariate models analyzing independent factors of NCDs are presented in Table 7. Multivariate Model 1 showed the following independent factors of NCDs (OR, *P* value): female gender (13.91, 0.049), divorced status (0.00, 0.041), poor education [illiterate (136.16, 0.004), primary school

Table 3: Lifestyle and other clinical parameters (*n*=236)			
Parameter	**Category**	**Frequency**	**Percentage**
Medical history			
Previously diagnosed cognitive disorders	Alzheimer's Disease	2	0.8
Other Comorbidities[§]	Hypertension	152	64.4
	Dyslipidemia	30	12.7
	Coronary artery disease	31	13.1
	Chronic kidney disease	27	11.4
	Stroke	14	5.9
	Head trauma	9	3.8
	Sleep apnea	55	23.3
	Other	15	6.4
No. other medications	0	111	47.0
	1	51	21.6
	2	41	17.4
	3+	34	14.4
Physical disability[§]	Hearing impairment	60	25.4
	Visual impairment	122	51.7
	Speech problem	14	5.9
	Difficulty walking	55	23.3
	Upper limb motor disability	8	3.4
Psychological health[§]	Stress/Anxiety	90	38.1
	Depression	66	28.0
	Phobia (neurosis)	16	6.8
	Obsessive compulsive disorder	2	0.8
	Post-traumatic stress disorder	2	0.8
	Other	3	1.3
Family psychiatric history[§]	Dementia	1	0.4
	Depression	26	11.0
	Psychosis	2	0.8
	Mental retardation	6	2.5
Lifestyle factors			
Eating habits	Normal	118	50.4
	Healthy	30	12.8
	Unhealthy	86	36.8
Exercise	Regular	119	51.3
	Irregular	55	23.7
	None/sedentary	58	25.0
BMI (kg/m²)	Underweight (<18.5)	9	3.9
	Normal weight (18.5-24.9)	110	47.1
	Overweight (25.0-29.9)	98	42.1
	Class I Obesity (30.0-34.9)	10	4.3
	Class II Obesity (35.0-39.9)	4	1.7
	class III obesity (40+)	2	0.9
Smoking status	Nonsmoker	180	78.6
	Quitter	30	13.1
	Currently Smoking	19	8.3
Sleep quality	Satisfactory	59	26.2
	Moderate	110	48.9
	Poor	56	24.9

[§]More than one category may apply to one patient; ADPF: Association of Diabetic Patients Friends; KAUH: King Abdulaziz University Hospital

(59.08, 0.011), middle school (31.77, 0.035), longer duration of diabetes (>10 years: [12.66, 0.008]), abnormal capillary glucose result on last measurement (7.57, 0.012), difficulty walking (0.15, 0.014), sedentary lifestyle (29.00, <0.001), and being cigarette quitter (0.06, 0.011). The model explained 45.4% of the variance of the dependent variable. Multivariate Model 2 showed the following independent factors of NCDs (OR, *P* value): longer duration of diabetes [>10 years: (6.19, <0.001)], age at T2DM diagnosis (1.09, <0.001), sedentary lifestyle (4.58, <0.003), and being cigarette quitter (0.15, 0.006). The model explained 32.5% of the variance of the dependent variable. Multivariate Model 3 showed the following independent factors of NCDs (OR, *P* value): married (0.06, 0.036), divorced (0.00, 0.004), and widowed (0.06, 0.040) statuses,

Table 4: Sociodemographic factors associated with neurocognitive dysfunctions among diabetic patients (*n*=236)

Parameter	Category	Normal		Abnormal		Statistics (df)	*P*
		n	%	*n*	%		
Gender	Male	68	73.9	24	26.1	5.46 (1)	0.020*
	Female	85	59.0	59	41.0		
Age (years)	Mean, SD	57.79	7.73	64.89	10.57	5.90 (234)	<0.001*
Marital Status	Single	5	71.4	2	28.6	17.25 (3)	0.001*
	Married	99	69.7	43	30.3		
	Divorced	20	87.0	3	13.0		
	Widowed	29	45.3	35	54.7		
No. Children	None	7	53.8	6	46.2	5.38 (3)	0.146
	1-3	37	72.5	14	27.5		
	4-6	62	69.7	27	30.3		
	7+	47	56.6	36	43.4		
Educational Level	Illiterate	42	45.2	51	54.8	33.29 (4)	<0.001*
	Primary	44	66.7	22	33.3		
	Middle school	26	81.3	6	18.8		
	Secondary	20	90.9	2	9.1		
	University+	21	91.3	2	8.7		
Nationality	Saudi	113	53.5	65	36.5	0.58 (1)	0.448
	Non-Saudi	40	69.0	18	31.0		
Residency area	Urban	107	71.3	43	28.7	10.90 (1)	0.001*
	Rural/Country	35	48.6	37	51.4		
Occupation	Employed	19	82.6	4	17.4	11.51 (3)	0.009*
	Housewife	72	58.1	52	41.9		
	Unemployed	15	57.7	11	42.3		
	Retired	43	79.6	11	20.4		
Monthly income (SAR)	<5 K	70	59.8	47	40.2	5.11 (3)	0.164
	5 K-10 K	56	72.7	21	27.3		
	10 K-15 K	15	68.2	7	31.8		
	>15K	3	100.0	0	0.0		

Values are frequencies, percentages; except if otherwise specified. Df: Degree of freedom; *Statistically significant result (*P*<0.05)

poor educational level [illiterate (15.42, 0.006), primary (7.28, 0.045)], longer duration of diabetes [>10 years: (9.37, 0.001)], age at T2DM diagnosis (1.13, 0.005), difficulty walking (0.35, 0.044), sedentary lifestyle (11.52, <0.001), and being ex-smoker (0.15, 0.013). The model explained 39.2% of the variance of the dependent variable.

Discussion

The present study reported an estimated prevalence of 35.2%, and 5.1% with severe impairment of neurocognitive functions after administrating MMSE to screen for NCDs. The typical profile associated with NCD was that of individuals with poor education (middle school and below and illiterates), widowed, older females residing in rural areas, with longer duration of diabetes, uncontrolled diabetes, who were likely to be diagnosed later, had a sedentary lifestyle and significant medical and psychiatric history notably cardiovascular comorbidities, depression, and physical and or sensorial disabilities. The analysis of three different multivariate regression models showed female gender, poor educational level, longer duration of diabetes, T2DM diagnosis at geriatric age, inadequate glycemic control, and sedentary lifestyle as the most significant independent risk factors for NCDs; whereas, being ex-smoker and having difficulty

walking were paradoxically found to be independent protective factors against NCDs.

In general, cognitive screening tests evaluate major aspects of the cognitive functions to detect significant abnormalities with high sensitivity. In clinical practice, several tools can be used to assess neurocognitive functions and screen for NCDs. The present study used the MMSE that examines several aspects including orientation, registration, attention and calculation, recall, and language and has strong diagnostic value in ruling out dementia.[18,23]

There is substantial evidence demonstrating a higher risk of NCDs among diabetic patients compared with nondiabetic individuals. Alaama *et al.*[24] estimated the prevalence of NCD among 171 diabetic patients and reported a significant association of NCD with geriatrics, poor education, waist circumference, HbA1c levels, geriatric depression score, and mean arterial blood pressure. Internationally, a meta-analysis of 19 longitudinal studies showed that diabetic individuals had a relative risk for developing Alzheimer's disease (1.46), vascular dementia (2.48), any dementia (1.51), and mild cognitive impairment (MCI) (1.21), over an average of 2–12 years of followup, as compared to controls.[3] A 2-year follow-up, a retrospective longitudinal study

Parameter	Category	Neurocognitive assessment					
		Normal		Abnormal		Statistics (df)	P
		n	%	n	%		
Diabetes assessment							
Time since diagnosis (years)	Up to 10	83	75.5	27	24.5	10.20 (1)	0.001*
	>10	70	55.6	56	44.4		
Age at diagnosis (years)	Mean, SD	44.40	10.26	49.49	11.81	3.45 (234)	0.001*
Do you see the doctor regularly for diabetes?	Yes, since the diagnosis	108	65.9	56	34.1	2.72 (2)	0.257
	Yes, but not since diagnosis	27	54.0	23	46.0		
	Yes, just recently	10	71.4	4	28.6		
Oral antidiabetic agent	No	26	59.1	18	40.9	0.78 (1)	0.337
	Yes	127	66.1	65	33.9		
Insulin	No	80	69.0	36	31.0	1.71 (1)	0.191
	Yes	73	60.8	47	39.2		
Diet	No	128	63.7	73	36.3	0.79 (1)	0.376
	Yes	25	71.4	10	28.6		
Last capillary glucose measure	Today	53	70.7	22	29.3	8.52 (3)	0.036*
	<1 week	57	73.1	21	26.9		
	>1 week	37	52.1	34	47.9		
	Never	4	66.7	2	33.3		
Last measure level	Normal	84	74.3	29	25.7	10.25 (2)	0.006*
	Abnormal	38	52.1	35	47.9		
	Do not know	26	59.1	18	40.9		
Diabetes control status	Uncontrolled or do not know	40	52.6	36	47.4	8.97 (2)	0.011*
	Moderately controlled	77	67.5	37	32.5		
	Well controlled	36	78.3	10	21.7		
Own a glucometer	No	21	63.6	12	36.4	0.02 (1)	0.903
	Yes	123	64.7	67	35.3		
Last HbA1c level (%)	<7	48	84.2	9	15.8	14.60 (1)	<0.001*
	>=7	61	54.5	51	45.5		
Diabetes complications							
Retinopathy	No	114	66.3	58	33.7	0.87 (2)	0.649
	Suspected	29	59.2	20	40.8		
	Confirmed	10	66.7	5	33.3		
Neuropathy	No	125	65.4	66	34.6	0.27 (2)	0.872
	Suspected	21	63.6	12	36.4		
	Confirmed	7	58.3	5	41.7		
Nephropathy	No	121	65.1	65	34.9	0.23 (2)	0.891
	Suspected	23	62.2	14	37.8		
	Confirmed	9	69.2	4	30.8		
Cardiovascular	No	119	70.8	49	29.2	9.29 (2)	0.010*
	Suspected	23	48.9	24	51.1		
	Confirmed	11	52.4	10	47.6		

Table 5: Diabetes-related factors associated with neurocognitive dysfunction (*n*=236)

Values are frequencies, percentages; except if otherwise specified. Df: Degree of freedom; * statistically significant result (*P*<0.05)

among 377,838 US seniors with diabetes found ~4% incidence of dementia,[25] which is very low as compared to the findings in this study. Similar to the findings in this study, a prospective cohort study from the USA showed 54% cases of executive dysfunctions, 33% of memory dysfunctions; whereas, 16% had both disorders.[26] In India, a cross-sectional study estimated, 35.6% prevalence of NCDs among diabetic patients using MMSE, and two-third of the cases had mild forms,[27] which is very similar to the findings of this study.

On the other hand, the prevalence of NCDs in the present study is comparable to that reported in a local community-based study among geriatrics (aged 60 and above).[28] The study used the Montreal Cognitive Assessment (MoCA) test and detected 38.6% cases of mild cognitive impairment and 6.4% cases of dementia. The studied population showed a high prevalence of diabetes, hypertension, dyslipidemia, and depression. Moreover, the use of standard cut-off detected a prevalence of NCDs as high as 72.5%.[28] In contrast, the global prevalence of dementia in geriatrics was estimated between 5% and 7% and was higher in developing countries[29,30]; whereas regional estimates among Arabic-speaking populations showed highly variable figures of NCDs prevalence ranging between 4.4% and 32%.[31-33] These high and heterogenous figures of NCDs found in the present

Table 6: Lifestyle and other clinical factors associated with neurocognitive dysfunctions among diabetic patients (*n*=236)

Parameter	Category	Neurocognitive assessment					
		Normal		Abnormal		Statistics (df)	*P*
		n	%	*n*	%		
Medical history							
Hypertension	No	65	77.4	19	22.6	9.01 (1)	0.003*
	Yes	88	57.9	64	42.1		
Dyslipidemia	No	137	66.5	69	33.5	1.99 (1)	0.158
	Yes	16	53.3	14	46.7		
Coronary artery disease	No	137	66.8	68	33.2	2.74 (1)	0.098
	Yes	16	51.6	15	48.4		
Chronic kidney disease	No	136	65.1	73	34.9	0.05 (1)	0.829
	Yes	17	63.0	10	37.0		
Stroke	No	149	67.1	73	32.9	8.58 (1)	0.007*F
	Yes	4	28.6	10	71.4		
Head trauma	No	148	65.2	79	34.8	0.35 (1)	0.724F
	Yes	5	55.6	4	44.4		
Sleep apnea	No	119	65.7	62	34.3	0.29 (1)	0.593
	Yes	34	61.8	21	38.2		
Other comorbidity	No	144	65.2	77	34.8	0.16 (1)	0.781F
	Yes	9	60.0	6	40.0		
Psychiatric comorbidities							
Anxiety/stress	No	97	66.4	49	33.6	0.43 (1)	0.510
	Yes	56	62.2	34	37.8		
Depression	No	117	68.8	53	31.2	4.25 (1)	0.039*
	Yes	36	54.5	30	45.5		
Phobia	No	144	65.5	76	34.5	0.55 (1)	0.457
	Yes	9	56.3	7	43.8		
OCD	No	152	65.0	82	35.0	0.20 (1)	1.000F
	Yes	1	50.0	1	50.0		
PTSD	No	152	65.0	82	35.0	0.20 (1)	1.000F
	Yes	1	50.0	1	50.0		
Other psychiatric comorbidity	No	153	65.7	80	34.3	5.60 (1)	0.042*F
	Yes	0	0.0	3	100.0		
Disabilities							
Hearing impairment	No	127	72.2	49	27.8	16.31 (1)	<0.001*
	Yes	26	43.3	34	56.7		
Visual impairment	No	83	72.8	31	27.2	6.15 (1)	0.013*
	Yes	70	57.4	52	42.6		
Speech problems	No	150	67.6	72	32.4	12.30 (1)	0.001*F
	Yes	3	21.4	11	78.6		
Difficulty walking	No	127	70.2	54	29.8	9.70 (1)	0.002*
	Yes	26	47.3	29	52.7		
Upper limb motor disability	No	151	66.2	77	33.8	5.76 (1)	0.024*F
	Yes	2	25.0	6	75.0		
Lifestyle factors							
Eating habits	Normal	80	67.8	38	32.2	3.10 (2)	0.212
	Healthy	22	73.3	8	26.7		
	Unhealthy	50	58.1	36	41.9		
Exercise	Regular	95	79.8	24	20.2	24.55 (2)	<0.001*
	Irregular	30	54.5	25	45.5		
	None/sedentary	26	44.8	32	55.2		
Overweight or obesity	No	78	65.5	41	34.5	0.15 (1)	0.704
	Yes	72	63.2	42	36.8		

Contd...

Table 6: Contd...						
Parameter	**Category**	**Neurocognitive assessment**				
		Normal		**Abnormal**		**Statistics (df)**	**P**
		n	**%**	***n***	**%**		
Smoking status	Nonsmoker	110	61.1	70	38.9	6.08 (2)	0.048*
	Quitter	23	76.7	7	23.3		
	Currently Smoking	16	84.2	3	15.8		
Sleep quality	Satisfactory	35	59.3	24	40.7	6.00 (2)	0.050
	Moderate	80	72.7	30	27.3		
	Poor	31	55.4	25	44.6		

Df: Degree of freedom; *statistically significant result (*P*<0.05); test used: ‡Fisher's exact test, otherwise Chi-square test; OCD: Obsessive-compulsive disorders; PTSD: Post-traumatic stress disorder

Table 7: Independent factors of neurocognitive disorders (*n*=236)					
Predictor	**Level**	**OR**	**95% CI**		**P**
MODEL 1: All significant variables in bivariate analysis					
Sociodemographic predictors					
Gender	Male	Ref	1.01	192.37	0.049*
	Female	13.91			
Age	(years)	0.99	0.88	1.12	0.909
Marital status	Single	Ref			0.034*
	Married	0.02	0.00	12.84	0.243
	Divorced	0.00	0.00	0.74	0.041*
	Widowed	0.01	0.00	7.47	0.178
Educational level	Illiterate	136.16	4.97	3730.21	0.004*
	Primary	59.08	2.57	1359.44	0.011*
	Middle school	31.77	1.27	793.56	0.035*
	Secondary	0.04	0.00	84.40	0.409
	University+	Ref			0.026*
Diabetes-related predictors					
Time since diagnosis (years)	Up to 10	Ref			
	>10	12.66	1.95	82.35	0.008*
Age at diagnosis	(years)	1.12	1.00	1.26	0.051
Last capillary glucose measured	Today	Ref			0.064
	<1 week	1.12	0.27	4.64	0.880
	>1 week	4.57	1.06	19.74	0.042
	Never	0.08	0.00	7.50	0.277
Last capillary glucose result	Normal	Ref			0.042*
	Abnormal	7.57	1.57	36.51	0.012*
	Do not know	2.94	0.55	15.63	0.206
Medical history					
Difficulty walking	Yes	0.15	0.03	0.68	0.014*
Lifestyle predictors					
Exercise	Regular	Ref			0.001*
	Irregular	5.68	1.35	23.88	0.018*
	None/sedentary	29.00	5.27	159.48	<0.001*
Smoking status	Nonsmoker	Ref			0.034*
	Quitter	0.06	0.01	0.53	0.011*
	Currently Smoking	0.36	0.04	3.27	0.361
MODEL 2: Excluding sociodemographic factors					
Diabetes-related predictors					
Time since diagnosis (years)	Up to 10	Ref			
	>10	6.19	2.46	15.58	<0.001*
Age at diagnosis	(years)	1.09	1.04	1.15	<0.001*
Lifestyle predictors					
Exercise	Regular	Ref			0.009*
	Irregular	2.36	0.96	5.79	0.060
	None/sedentary	4.58	1.70	12.35	0.003*

Contd...

Predictor	Level	OR	95% CI		P
			Table 7: Contd...		
Smoking status	Nonsmoker	Ref			0.009*
	Quitter	0.15	0.04	0.59	0.006*
	Currently Smoking	0.25	0.05	1.32	0.102
MODEL 3: Factors that showed significance in Model 1					
Sociodemographic predictors					
Gender	Male	Ref			
	Female	2.41	0.89	6.49	0.083
Age	(years)	0.99	0.91	1.08	0.855
Marital status	Single	Ref			0.040*
	Married	0.06	0.01	0.83	0.036*
	Divorced	0.00	0.00	0.22	0.004*
	Widowed	0.06	0.00	0.88	0.040*
Educational level	Illiterate	15.42	2.20	108.29	0.006*
	Primary	7.28	1.04	50.78	0.045*
	Middle school	3.28	0.36	29.61	0.290
	Secondary	0.94	0.07	13.27	0.962
	University+	Ref			0.007*
Diabetes-related predictors					
Time since diagnosis (years)	Up to 10	Ref			
	>10	9.37	2.39	36.80	0.001*
Age at diagnosis	(years)	1.13	1.04	1.22	0.005*
Medical history					
Difficulty walking	Yes	0.35	0.13	0.97	0.044*
Lifestyle predictors					
Exercise	Regular	Ref			<0.001*
	Irregular	3.02	1.15	7.96	0.025
	None/sedentary	11.52	3.81	34.77	<0.001*
Smoking status	Nonsmoker	Ref			0.036*
	Quitter	0.15	0.03	0.67	0.013*
	Currently Smoking	0.40	0.06	2.50	0.325

OR: Odds ratio; 95%CI: 95% confidence interval; Ref: value used as reference to calculate OR; *statistically significant result (*P*<0.05)

study are likely due to the use of highly sensitive tools and evaluation methods with limited specificity. This highlights the need to refer the positively screened individuals for specialized psychiatrist evaluation to confirm the diagnosis and rule out false positives.

Findings from the present study demonstrated the significant association of NCDs with a panel of factors, delineating a high-risk sociodemographic profile associating older age, female gender, poor or no education, and rural residence setting. Besides, several clinical factors were identified including sedentary lifestyle, longer duration of diabetes, poor glycemic control, history of depression, cardiovascular morbidities, hypertension, stroke, and physical disabilities. However, the most significant among these factors were female gender, poor or no education, longer duration of diabetes, older age at T2DM diagnosis, inadequate glycemic control, and sedentary lifestyle. Some of the previous studies also demonstrated these factors to be associated with NCDs.[24,25,34]

Higher education is consistently associated with higher scores at cognitive test scores, whereas poor or no education is often reported to be associated with a higher prevalence of NCDs and dementia in various populations.[20,35] From another perspective,

analysis of the aforementioned high-risk profile including no or poor education, besides other sociodemographic factors, suggests that the development of NCDs may result from a combination of poor health literacy and reduced access to health care. This combination leads to delayed diagnosis of T2DM, inadequate follow-up and glycemic control, inappropriate screening for comorbidities and complications, and impaired self-management. Thus, appropriate measures should be undertaken to enhance the health care offer and patient education among these high-risk subpopulations, both at the institutional and national levels.

The role of cardiovascular comorbidities, notably cerebrovascular diseases, is important in the pathogenesis of NCDs and dementia in diabetes patients. Neurocognitive decline is a commonly explored issue in stroke survivors. In Saudi Arabia, ischemic stroke represents ~75% to ~87% of stroke subtypes, with diabetes and hypertension accounting for the most important risk factors.[36] The development of vascular dementia, which is the most frequent subtype of NCDs in diabetes, is significantly linked to macro-and diabetes microvascular pathological processes leading to brain infarcts or vessel pathology of the central nervous system. These complications are potentiated

by other metabolic and systemic co-morbid conditions notably hypertension and dyslipidemia.[12]

Regarding psychiatric comorbidity, depression is known as a strong cofactor of NCDs in diabetic patients, which further impairs diabetes self-management and compromises the prognosis.[37] Depression can also be one of the presenting symptoms of dementia, especially in geriatrics, which highlights the need to screen for NCDs in all geriatrics with depression.[38]

One of the limitations observed during the administration of the MMSE was the likelihood of confounding effect of educational level on understanding and answering the test questions. The use of MMSE is intended for screening purposes; therefore, the positive cases should be completed by referral to a psychiatrist consultation to confirm the diagnosis. Moreover, the present study is limited by the disproportionate distribution of participants across the included PHCCs, as 50.4% were recruited from one of the five centers, which may explain the high percentage of illiterates, housewives, and geriatrics in the sample. This had probably resulted in an overestimated NCDs case detection and may limit generalization of the findings to the target population. Additionally, recall bias may be introduced regarding some cofactors such as duration of the disease, history, with regards to the study design.

The results provide insight and pave the path for the physicians at primary health care centers, which are considered as the significant centers for counseling of patients and prevention of diseases. The elderly age group is rising in Saudi Arabia and the burden of diabetes is also increasing as reported in the literature, and the neurocognitive complications are more often accoutred in elderly individuals. By keeping in view, the current circumstances, the counseling of patients at primary health care setups is the need of the time so that the behavioral changes in the community can be initiated and implemented along with the preventive strategies, and the physicians at PHC might play a vital role in this regard.

Key messages

The study was conducted at primary health care centers in Jeddah in which two stage cluster sampling technique was employed. A stringent exclusion and inclusion criterion was followed for the recruitment of subjects, and an extensive questionnaire was applied to achieve the objective of the study. The statistical regression model was used for analysis so that the bias and confounders can be controlled for the generalizability of results and also might be helpful to predict the magnitude of the problem. The study has estimated the prevalence of NCDs in a representative sample of diabetic patients, which showed that the prevalence of NCDs was significantly higher among geriatrics, individuals with poor or no education, females, people residing in rural areas, delineating a high-risk sociodemographic profile.

Conclusions

The administration of MMSE among middle-aged and geriatric T2DM patients suggests that over one-third of this population is had NCDs, and ~5% had severe impairment of neurocognitive functions. The prevalence of NCDs was significantly higher among geriatrics, individuals with poor or no education, females, people residing in rural areas, delineating a high-risk sociodemographic profile. Depression is a silent condition that is highly associated with NCDs among diabetic patients, and maybe one of the presenting symptoms of dementia. Further improvements should be achieved to enhance the care offered to diabetic patients by improving glycemic control, screening for comorbidities, and early detection of neurocognitive decline.

Conflicts of interest

There are no conflicts of interest.

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