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The Value of Collateral History in Screening for Mild Cognitive Impairment in Elderly with Diabetes Mellitus in Outpatient Clinics

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Abstract

Background: Cognitive decline is a common consequence of type 2 Diabetes Mellitus (T2DM) in elderly patients. It often remains an overlooked diabetic complication, especially in its preclinical stage -the mild cognitive impairment (MCI) - that is the transitional state for both Alzheimer's and vascular dementias. MCI has been addressed as the target stage for risk reduction and therapeutic trials. The main barrier for accurate and early detection of early cognitive impairment is the time consuming neuropsychological testing that requires qualified skilled training which the primary health care providers often lack. Therefore, there is a strong need for an accurate and less time consuming screening tools that can be administered with minimal training compared to the current available neuropsychological tests.

Objective*:* to assess the usability of standardized collateral history as a simple screening tool for MCI in elderly patients with T2DM.

Methods*:* A case–control study included 90 elderly diabetic participants (≥ 60 years), divided into 45 cases with MCI (40 amnestic and 5 non- amnestic) and 45 controls. Patients with depression, dementia, delirium, previous head trauma, any central nervous system pathology, users of the anticholinergic drugs, or those refused to participate in the study were excluded. Each patient underwent neuropsychological assessment using the Arabic Mini-mental state examination and a structured objective neuropsychological battery composed of (the logical memory test, forward and backward digit span tests, category fluency test, go/no go test, stick design test, and second-order belief (John and Mary story)). Each patient had a reliable informant to complete the collateral history form which included 11 questions that cover all neurocognitive domains. The learning/ memory, and attention were the most presented domains with 4 and 3 items, respectively.

Results*:* The collateral history scores were higher in MCI diabetics versus controls (P = <0.0001), it had excellent accuracy to discriminate MCI (area under curve = 0.935, P = <0.0001). At cut-off ≥ 3, sensitivity and specificity values were 88.89% and 95.56%, respectively. The collateral history scores had moderate to strong inverse correlation to other used neuropsychological tests (rho=-0.659 to -0.806). The internal consistency of the collateral history scored 0.969.

Conclusion: The collateral history is a simple, reliable, and accurate screening tool for detecting MCI among aged diabetics.

Key words: Mild cognitive impairment, collateral history, cognitive screening

Background

Cognitive dysfunction is a common and debilitating complication associated with type 2 diabetes mellitus (T2 DM). Therefore, most of the clinical guidelines for diabetes management in elderly paid a great attention to cognitive screening for elderly diabetics.[1–6] However, the recommended screening tools have not

been standardized across different guidelines. Moreover, the development of cognitive screening and management strategies failed to keep the pace with those developed for other diabetic complications.[7]

MCI is the preclinical transitional state of Alzheimer's and vascular dementia. Thus, it became the target for prevention[8], early treatment[9], and cognitive training trials.[10,11] Thus detection of subtle cognitive impairment in its earliest stages remains a corner stone for these clinical interventions.

Many different brief screening tests for cognitive impairment are available,[12–16] yet; various barriers facing their dissemination in primary care and diabetes clinics. Most of these widely used tools are time consuming and require qualified skilled training for their administration and interpretation.[12–15]. Moreover, they are literacy dependent [17,18]and mostly affected by the pre-morbid cognitive reserve. [19]

Using collateral history to describe cognitive change is an important alternative for cognitive screening mainly in primary settings because the informant view is not affected by patients' educational level and it acknowledges the decline from premorbid state. The Informant Questionnaire for Cognitive Decline in the Elderly (IQCODE) is one of the most commonly used tools, [20] it was validated for MCI screening.[21] however, the IQCODE uses a Likert scale survey, the intervals between points do not translate equal changes for all respondents, for example, the differences between a bit improved, not much change, and a bit worse.

Therefore, in this study we evaluated the accuracy of an informant based screening tool that uses closed questions including all cognitive domains presented in the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) criteria for the diagnosis of MCI among elderly diabetics.[22]

Methods

A case control study was conducted to assess the accuracy of collateral history taking in diagnosing mild cognitive impairment among elderly diabetic patients compared to structured objective neuropsychological battery.

The study sample comprised 90 participants with diabetes aged 60 years and above, attending the Geriatric and the Neurology outpatient clinics in Ain Shams University Hospital, Cairo, Egypt. We excluded those with any CNS pathology, or trauma, those with dementia, depression, delirium, using anticholinergic drugs, or refused to participate in the study. Each patient had a reliable informant to complete the collateral history form.

The participants were allocated into three groups according to their cognitive performance into amnestic MCI, Non- amnestic MCI, and those with normal cognition (Controls). MCI was diagnosed based on the criteria of the DSM-5.[22]

Each patient underwent neuropsychological assessment using Arabic Mini-mental state examination[23] and structured objective neuropsychological battery.

Arabic Mini-mental state examination A-MMSE[23]: it has a total score of 30. It assesses orientation, attention, calculation, registration, recall, language, and figure copying.

The neuropsychological battery consisted of the following tests: logical memory (LM) subtest of Wechsler Memory Scale Fourth Edition (WMS–IV) [24], forward and backward digit span [25], Verbal fluency test (semantic animal category)[26], go/no go test[27], stick design test [28], and second-order belief (John and Mary story)[29]. Cut off scores for MCI diagnosis is ≥ 1.5 standard deviation (SD) below the normative data corrected for age, gender, and educational level [30].

Description of the neuropsychological battery items:

logical memory (LM) subtest of Wechsler Memory Scale Fourth Edition (WMS–IV):[24] verbal recall of auditory presented story passage and then immediately recall all details they could remember. Then, a second story was presented followed by immediate recall. 30-minutes later the subject performed a delayed recall test. (Subjects were forewarned of a delayed recall test).

Forward and backward digit span:[25] For each part, the administrator presented a series of numbers at the rate of about one per second. For digits forward, the test starts with a sequence of three numbers and continues to a maximum of eight numbers, while in digits backward, the test begins with series of two numbers and continues to a maximum of seven numbers. Patients are allowed for two trials at each series length, and the test continues until both trials of a series length are failed. Each successful series is awarded by one point. The total score is the sum of all the trials answered correctly for both digits forward and digits backward.

Verbal fluency test (semantic animal category):[26] Each participant was asked to tell all the animals that he knew as fast as possible in one minute. The number of correct, non-repeated responses represented the total score. The animal category was chosen for this test, because it could be used in those with low formal education normative data for Egyptian elderly was adapted from Abdel Aziz et al., 2016.[26]

Go no Go test:[27] it is a measure of executive function, it assess frontal lobe function specifically the inhibitory control. The examiner asked the patient to place a hand on the table. Then the examiner tapped under the table, asked the patient to tap when the examiner tap once and not to tap when examiner tap twice. He showed the patient how it's done and then the test was performed. He made sure that the patient has understood the instruction, by tapping a series of three trials is run: 1-1-1 followed by 2-2-2. Then the examiner performed the following sequence: 1-1-2-1-2-2-2-1-1-2. The score ranges between 0 when the patient

tap as the examiner for at least 4 consecutive times and 3 when there was no errors.

Stick design test (visuospatial)[28] it is a non grapho-motor assessment of visuo- constructional ability. The patients are allowed to reproduce geometric figures using match sticks. A representation of an arrangement of four wooden matches was printed on a page. The designs included a square, a triangle with stem, a chevron, and a rake-like figure. For each item the examiner constructed the figure and then asked the patient to copy.

Second-order belief (John and Mary story):[29]

False – belief tasks, the subject was asked to identify the false belief of one person based on the thoughts of another. The story involved two characters (John and Mary), who were informed (independently) about placing an object in a new place. Now both John and Mary knew where the object was but John's second-order belief is wrong about Mary's belief: "John *thinks* Mary *thinks* the van is still at the old place" testing was by asking "Where does John think Mary will go for ice cream?" the correct response should account for John's wrong belief.

Collateral history form:

The authors selected 11 questions that represented the most commonly reported cognitive symptoms of patients with MCI attending the clinic. During the selection of these questions, all neurocognitive domains were included (attention, memory, perceptual motor, executive, social cognition, and language). It ask about situations that relate to everyday life. The form aims to assess cognitive decline independent of pre-morbid ability or educational level. A closed question (yes/no) format was preferred for ease of administration and simplicity of scoring. Each yes item scored one, with a total score of 11. The learning/ memory, and attention were the most presented domains with 4 and 3 items, respectively (Table 1).

Statistical analysis

Data were analyzed using SPSS package version number 20. Quantitative data were described as median and inter quartile range (IQR) values. Kruskal-Wallis rank sum test was used for comparing quantitative variables between groups. Qualitative data were expressed as frequencies (n) and percentage (%). Fisher's exact test and the chi-square test were used to test association between qualitative variables. The correlation between two quantitative variables was carried out using Spearman's correlation coefficient. The internal consistency of the scales was measured by the Cronbach's alpha P-value ≤ 0.05 was considered significant. For the receiver operating characteristic curves, we used MedCalc Statistical Software version 18.9.1 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2018).

Ethical consideration

Informed consent was obtained from every elder participated in this study. The study methodology was reviewed and approved by the Research Review Board of the Geriatrics and Gerontology Department, Faculty of medicine, Ain Shams University as a part of thesis protocol approval for master degree fulfillment.

Table 1: the collateral history items and their related cognitive domains

item	Cognitive domain
Q1: Is he/she able to track someone or follow instructions successfully to a certain place?	Learning and visuo-spatial
Q2: Does he/she understand facial expressions and express emotions as sympathy, joy or sad suitable for current situation?	Social cognition
Q3: Does he/she forget taking medications?	memory
Q4: Can he/she keep track of movie or a TV series events and characters?	Complex attention, Learning and memory
Q5: Does he/she tell the same story to the same people repeatedly?	Learning and memory
Q6: Does he/she prefer to use to do lists and reminders than usual?	Learning and memory
Q7: Does he/she find it difficult to find a specific word or expression, for example, does he prefer to say (my daughter) instead of telling (her name)?	Language
Q8: Is it difficult for him/her to make decisions?	executive function,
Q9: Did he/she become less fond of family or friends gatherings than usual?	Social cognition
Q10: Does he/she need repeated instructions to perform a task?	Complex attention, executive function,
Q11: Does he/she take longer duration to accomplish usual tasks?	Complex attention

Results:

The sociodemographic data of the participants was previously published.[31] The mean age of the participants was 65.7 ± 3.9 years old. Females accounted for 37.8% of the subjects. There was no significant difference between cases and controls regarding gender (*P* = 0.38).

Most of the study participants were illiterate. They accounted for 32 (71.1%) and 28 (62.2%) among cases with MCI and those with normal cognition, respectively. (P= 0.670)

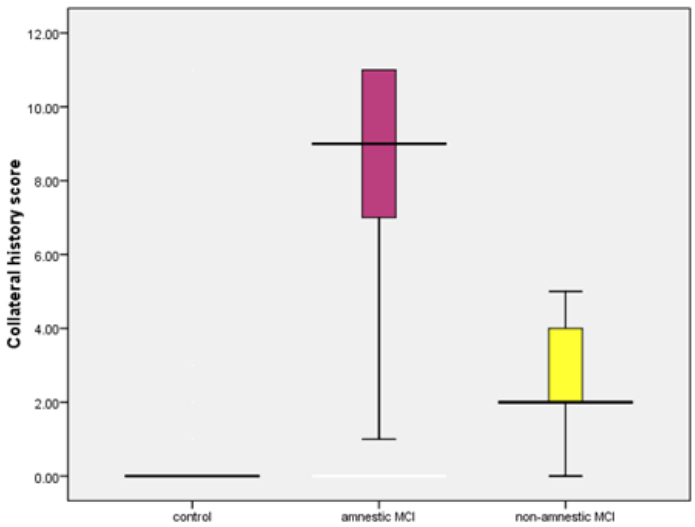
Table 2 showed that the collateral history scores were higher in MCI diabetics versus controls (P = <0.0001), moreover; all other neuropsychological tools were significantly affected in MCI groups compared to controls. The median A-MMSE scores were 27(26-28), 23(22-25), and 26(24-27) among controls, amnestic, and non-amnestic MCI, respectively.

The median collateral history scores were 9, 2, and 0 for amnestic, non-amnestic MCI, and controls, respectively ***(figure 1).***

Table 3 showed that the collateral history scores had moderate to strong inverse correlation to other used neuropsychological tests (rho=-0.659 to -0.806).

The strength of the correlation was interpreted according to values used by **(Bland and Altman, 2011)** [32]

Figure 1: median collateral history score among the three groups:



The median collateral history scores were 9, 2, and 0 for amnestic, non-amnestic MCI, and controls, respectively.

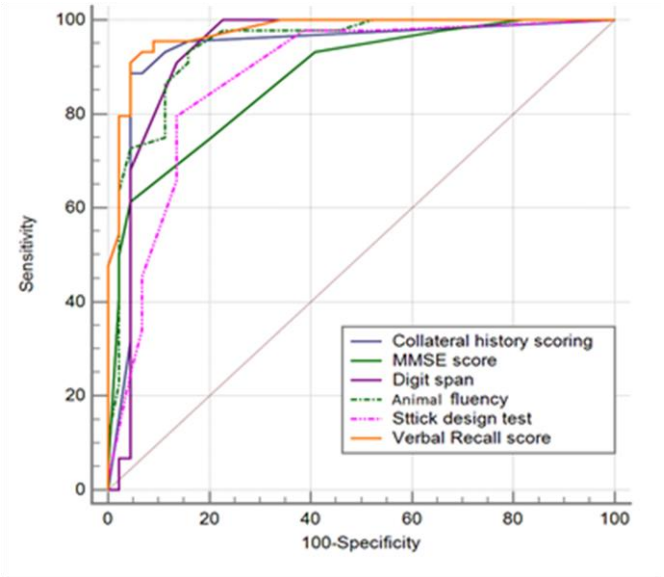
The strongest correlation was between collateral history score and verbal recall (rho=0.806).

Table [4] showed that the internal consistency of the collateral history was excellent (Cronbach's Alpha=0.969). The corrected item total correlations were moderate to strong (ranged between 0.673 and 0.918).

Table 5 and figure 2 showed that, the collateral history had excellent accuracy to discriminate MCI (area under curve = 0.935, P = <0.0001). At cut-off ≥ 3, sensitivity and specificity values were 88.89% and 95.56%, respectively.

It was more accurate than A-MMSE (AUC=0.875, Cut off ≤24 had sensitivity and specificity values of 60.00% and 95.56%, respectively. The collateral history had a comparable accuracy to all items of the objective neuropsychological battery.

Figure 2: ROC curve analysis for the accuracy of different tools for detecting MCI



The collateral history had excellent accuracy to discriminate MCI (area under curve = 0.935, P = <0.0001). At cut-off ≥ 3, sensitivity and specificity values were 88.89% and 95.56%, respectively. While, A-MMSE had AUC=0.875, Cut off ≤24 had sensitivity and specificity values of 60.00% and 95.56%, respectively.

Table (2): The neuropsychological assessment tools among different groups

	MCI		Control N=45	P value
	Amnestic N=40	Non amnestic N=5		
A-MMSE median (IQR)	23(22-25)	26(24-27)	27(26-28)	<0.0001a
Collateral history score median (IQR)	9(7-11)	2(1-5)	0(0)	<0.0001 a
Digit span score median (IQR)	6(5-8)	8(6-9)	10(10-12)	<0.0001 a
Verbal recall score median (IQR)	14(12-19)	15(15-30)	37(32-42)	<0.0001 a
Animal fluency score median (IQR)	8(6-10)	11(9-11)	14(13-15)	<0.0001 a
Stick design score median (IQR)	8(4-9)	9(6-10)	11(10-12)	<0.0001 a
Go no Go score median (IQR)	2(1-2)	2(2-2)	3(3-3)	<0.0001 a
Abnormal John Mary story test n(%)	7(17.5%)	1(20%)	1(2.22%)	0.03b

a Kruskal-Wallis rank sum test , b Fisher's exact test

Table (3): the correlation between collateral history score and other neuropsychological tools:

variable	Rho	P value
A-MMSE	-0.695	<0.0001
Digit span	-0.680	<0.0001
Animal fluency	-0.709	<0.0001
Verbal recall	-0.806	<0.0001
Stick design	-0.659	<0.0001

Spearman's correlation

Table (4): The internal consistency of collateral history taking and its affection in different groups:

Cronbach's Alpha=0.969	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted	The studied sample			P value
Items			Amnestic MCI N=40	Non amnestic N=5	Control N=45	
Q1: Is he/she able to track someone or follow instructions successfully to a certain place?	0.690	0.971	19(47.5%)	0	2(4.44%)	<0.0001
Q2: Does he/she understand facial expressions and express emotions as sympathy, joy or sad suitable for current situation?	0.673	0.971	17(42.5%)	0	2(4.44%)	<0.0001
Q3: Does he/she forget taking medications?	0.890	0.965	34(85%)	1(20%)	2(4.44%)	<0.0001
Q4: Can he/she keep track of movie or a TV series events and characters?	0.918	0.964	37(92.5%)	2(40%)	3(6.66%)	<0.0001
Q5: Does he/she tell the same story to the same people repeatedly?	0.841	0.966	38(95%)	1(20%)	2(4.44%)	<0.0001
Q6: Does he/she prefer to use to do lists and reminders than usual?	0.915	0.964	39(97.5%)	2(40%)	6(13.33%)	<0.0001
Q7: Does he/she find it difficult to find a specific word or expression, for example, does he prefer to say (my daughter) instead of telling (her name)?	0.876	0.965	37(92.5%)	0	3(6.66%)	<0.0001
Q8: Is it difficult for him/her to make decisions?	0.889	0.965	31(77.5%)	0	3(6.66%)	<0.0001
Q9: Did he/she become less fond of family or friends gatherings than usual?	0.879	0.965	30(75%)	0	2(4.44%)	<0.0001
Q10: Does he/she need repeated instructions to perform a task?	0.880	0.965	38(95%)	4(80%)	0	<0.0001
Q11: Does he/she take longer duration to accomplish usual tasks?	0.843	0.966	36(90%)	4(80%)	3(6.66%)	<0.0001

Table (5): The accuracy of different tools for detecting MCI

	Cut off point	AUC	P value	Sensitivity	Specificity
Collateral history score	>3	0.935	<0.0001	88.89	95.56
MMSE score	≤24	0.875	<0.001	60.00	95.56
Immediate memory story a	≤7	0.958	<0.001	91.1	95.56
Delayed memory story a	≤3	0.962	<0.001	86.7	97.8
Immediate memory story b	≤8	0.966	<0.001	84.44	95.56
Delayed memory story b2	≤4	0.969	<0.001	91.1	95.56
Total verbal recall	≤22	0.974	<0.001	91.1	95.56
Animal fluency	≤11	0.944	<0.0001	88.89	88.89
Go no Go test	≤ 2	0.862	<0.0001	82.2	86.67
Total stick design	≤ 9	0.877	<0.0001	80.00	86.4
Digit forward	≤5	0.838	<0.0001	75.56	80
Digit backward	≤3	0.948	<0.0001	100	84.44
Total digit span	≤8	0.934	<0.0001	91.1	86.4

Discussion:

The present study confirmed that the designed collateral history questions score discriminated well between the MCI and normal cognition among a sample of elderly diabetics attending outpatient clinics. It had excellent accuracy to discriminate MCI (area under curve = 0.935, *P* = <0.0001). At cut-off ≥ 3, sensitivity and specificity values were 88.89% and 95.56%, respectively. The score has high internal reliability with Cronbach's alpha =0.969.

In our study, the collateral history score was better than the A-MMSE as a screening instrument for MCI. This may be due to the low educational level in our participants, as illiterate accounted for 32 (71.1%) of cases and 28 (62.2%) among controls. It has been previously reported that MMSE is literacy dependent tool. It has a high misclassification error for older adults who are illiterate.[33] The MMSE diagnostic cut offs are based on education-specific norms equations.[34,35].

The informant based questionnaires have the advantage of being literacy independent, informant's view has been used to construct the widely used IQCODE which was initially applied to the Australian population and has been reported as a reliable screening tool for dementia.[36] This was followed by its validation among those with low education in many populations with like Thai[37], Chinese[38], Brazilian[39], etc.

The IQCODE was also validated for screening MCI[21] and early Alzheimer's disease. [40]. However, the IQCODE uses a Likert scale survey, where the intervals between points do not translate equal changes for all respondents, for example, the differences between a bit improved, not much change, and a bit worse. Therefore, this study aimed to evaluate the accuracy of a brief informant questionnaire involving all cognitive domains that does not require qualified trained practitioner to administer. This is an attempt to disseminate cognitive screening in diabetic patients beyond skilled memory clinics to allow for better diabetes clinical management. The development of a standardized yet a simple way of including informant data into cognitive assessment allows for more primary physicians adherence to the clinical guidelines for diabetes management in the elderly and perform a comprehensive assessment for their diabetic patients. The tool is simple and can be administered in paper form, on the telephone, or in electronic format.

The simplicity of the collateral history score didn't come at the expense of its accuracy. Table 5 showed that it was more accurate than MMSE, it had a comparable accuracy to all the objective neuropsychological tests used for cognitive assessment in the current study.

However, the informant's view can be biased by the cognitive function and the mood of the informant and the subjective complaints of the patient. Therefore, prescreening of informants may be recommended. The age, degree of contact, mood, and cognitive ability of the informant, and the nature of the informant-patients relationship should be evaluated.[41].

This study has some limitations. First, CT/MRI brain was not performed so the score neuroimaging correlates was not available. Second, the prescreening of the informant was not performed, only the primary caregiver was allowed to complete the form. Thirdly, whether collateral history score alone would be sufficient for use in research setting needs further evaluation.

Moreover, further research is needed to determine the collateral history accuracy to identify older diabetic with dementia and to include the symptoms of severe neurocognitive decline.

Conclusion: collateral history is an accurate, reliable, and brief tool of MCI screening in the elderly with diabetes in clinical settings.

Conflict of interest: The authors declare no conflicts of interest with respect to the authorship and publication of this article.

Data availability: data and the Arabic form of collateral history will be provided upon request

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