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საქართველოს სამედიცინო სიახლენი

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8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხო-ური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი,წელი,ჟურნალის №,პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანე-ლის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა,მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა,რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შე-ჯერება ხდება სააგტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

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აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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Содержание:

# PREVALENCE OF COGNITIVE IMPAIRMENT AND ITS ASSOCIATED FACTORS AMONG TYPE 2DIABETIC PATIENTS: FINDING FROM A CROSS SECTIONAL STUDY IN IRAQ

**Israa M. Salih[1]\*, Harith Kh. Al-Qazaz[2].**

*[1]Nineveh Health directorate, Mosul, Iraq.*
*[2]Department of Clinical Pharmacy, College of Pharmacy, University of Mosul, Mosul, Iraq.*

**Abstract.**

**Background:** Diabetes mellitus is a metabolic condition characterized by chronic hyperglycemia and disturbance in body metabolic state. It is estimated that nearly half of patients with diabetes will suffer from cognitive impairment and impairment in the performance of daily functions. The aim was to determine the prevalence of cognitive impairment and its predictors among diabetics.

**Methods:** A cross-sectional study was conducted on type 2 diabetic patients attending the AL-Wafaa clinic in Mosul. A validated questionnaire Saint Louis University Mental Status Examination (SLUMS) was used to evaluate cognitive function. The recent value of FBS or RBS and HbA1c were attained from the patient's records.

**Results:** The result demonstrated that 90% had impaired cognitive function. No significant correlation between cognitive function and age, BMI, HbA1c, duration of diabetes, and duration of co-morbid disease. Significant correlation between cognitive function and RBS level. Significant differences were found between cognitive function and gender, smoking, educational level, employment, and monthly income. While no significant differences were found with the marital state. The differences between SLUMS scores and the type of medications used for diabetes also were examined and no significant differences were found.

**Conclusion:** Decline cognitive performance is common among diabetic patients, more than half had a cognitive function. It is associated with gender, smoking, educational level, employment, and monthly income. No association was reported with age, HbA1c, duration of diabetes, and medication used for diabetes.

**Key words.** Dementia, diabetes type 2, cognitive, glycemic control, HbA1c, SLUMS.

**Introduction.**

Diabetes mellitus is a heterogeneous group of diseases characterized by chronic hyperglycemia that is associated with end-organ dysfunction, damage, and failure, like the blood vessels, retina, kidney, heart, and nervous system. The estimated prevalence of diabetes by the International Diabetes Federation (IDF) was 366 million in 2011 and is expected to increase to 552 million by 2030 [1]. Cognitive impairment is the inability to remember, learn new things, concentrate, or make decisions that affect daily life and increases the burden on society due to functional disability and thus increased health care costs [2].

Diabetes mellitus is a recognized danger issue for cognitive impairment. Learning and memory, language, executive feature, complicated interest, perceptual-motor, and social cognition are all examples of cognitive capabilities. Mild cognitive impairment (MCI) represents an intermediate stage between normal cognition at a certain age and more serious deterioration of dementia [3]. Mild cognitive impairment can occur without meeting the whole diagnostic standards for dementia, which requires that the deficiencies interfere with day-by-day activities. Patients with diabetes are more likely to have cognitive problems [4].

With advancing age, the chances of developing cognitive impairment increase, but cases of cognitive impairment have been recorded in people with diabetes who are at a young age [5]. Diabetes associated with both subtypes of MCI (aMCI and naMCI) in middle-aged patients [6]. It is estimated that nearly half of patients with diabetes will suffer from cognitive impairment and impairment in the performance of daily functions [7]. Cognitive impairment leads to the inability to comply with instructions for the correct use of medications, proper diet, and exercise, which leads to irregular blood sugar, including the risk of hypoglycemia [8].

Several studies indicate that high blood sugar is linked to cognitive impairment, according to ACCORD MIND, an increase of 1%in HbA1c results in a 0.14 decrease in the mini-mental state examination [MMSE) score [9]. Brain cells utilized glucose as a primary source of energy. Some studies suggest that repeated episodes of hypoglycemia are associated with cognitive impairment [10]. The chronic hyperglycemia of diabetes increases the production of advanced glycation end products. Among these long-lived glycated proteins are neurofibrillary tangles and amyloid-beta plaque markers of Alzheimer's disease (AD). The metabolic sequelae of the formation of AGE includes oxidative stress, cell function impairment, and glucose hypometabolism. AGE affects neuronal cell functioning by a number of mechanisms like calcium influx, apoptosis, oxidative stress, and oxidative phosphorylation inhibition [11,12]. To determine the prevalence of cognitive impairment and its predictors among diabetics.

**Materials and methods.**

**Study design and setting:** Cross-sectional study by means of convenient sampling methods was conducted to collect the required number of patients for the study. Al-Wafaa diabetes center in Mosul. The study was conducted from December 2021 to April 2022. The study approval was obtained by the ethical committee of the Clinical Pharmacy Department at the College of Pharmacy, University of Mosul, and the ethical committee in the Nineveh Directorate of Health. All patients who agreed to participate in the study signed a consent form. The HbA1c level were obtained from the patient's record and FBS were measure for fasted patients otherwise RBS were measured. The cognitive function was assessed using a SLUMS questionnaire.

**Participants:** participants of both sex who were diagnosed with type 2 diabetes irrespective of the type of medication used or duration of diabetes. patients with psychiatric disorders, Patients on sleeping pills, pregnant women, and night shift workers were all excepted from the study.

**Sample size:** The required sample was determined using the Raosoft sample size calculator (http://www.raosoft.com/samplesize.html). The study population was calculated depending on the number of patients who visit the Al-Wafaa center. About 32000 patients attended the Al-Wafaa center annually about third of them had T1DM and were excluded. The remaining 21000 patients are considered as the total number used to calculate the required sample. According to Raosoft, the required number was 378 with an accepted margin of error of 5% and a confidence level of 95%. The final sample size which depended on this study was 380 patients.

**Research instruments:** The Arabic version of the SLUMS questionnaire was used for cognitive function examination in this study. It consists of two parts demographic information, and cognitive function as follows:

**1-Sociodemographic data:** It consist of age, sex, BMI, smoking, marital state, education level, monthly income, and information about diabetes like duration and type of medication used. Also, past medical history, history of other comorbid disease, duration and treatment used for it.

2- Cognitive function was examined in all the patients by the Saint Louis University Mental Status (SLUMS) is a screening tool for the cognitive state it consists of 11 items and a total score of 30 points and needs about 7 min. for administration. It consists of seven domains of assessment of cognition: attention, recall, orientation, fluency, calculation, visuospatial construction, and language. An excellent discriminator between normal cognition and mild cognitive changes is the 5-word delayed recall [13]. Arabic version of SLUMS was used in this study [14]. Many types of cognitive screening tests were available, but no one can be considered superior to another, for example, Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment are commonly used and required a high educational level. SLUMS is more convenient for the study population and available in many languages.

**Scale scoring:** SLUMS score is divided as follows:
For high school education.
1- Score from 27 - 30 Normal.
2- Score from 21 - 26 Mild neurocognitive disorder.
3- Score from 1 - 20 for dementia.
For less than high school education
1- Score from 25 - 30 Normal.
2- Score from 20 - 24 Mild neurocognitive disorder.
3- Score from 1 - 19 Dementia.
Since more than half of the study population had a low educational level (primary 58.4%) the cutoff point used was ≤ 24.

**Statistical analysis:** For data analysis, SPSS version 19 was used. For categorical variables Percentages and frequencies were used and for continuous variables Mean ± SD were used. To test the correlation between two continuous variables spearman was used and for continuous and two or more categorical variables Mann-Whitney U and Kruskall-Wallis H were used respectively. A p-value < 0.05 was considered as significant.

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## Results.

**Demographic characteristics of the study population:** The socio-demographic characteristics for a total of 380 patients were prescribed as follows: The age between 35 to 82 years with mean ± SD 55.47 ± 8.356 and the mean ± SD BMI was 29.69 ± 5.047. Most patients were married (98.7%) and 54.7% were men. The mean duration of diabetes in the study was 10.18 years and the mean HbA1c ± SD level of 8.68 ± 1.47 (Table 1). About 40% of participants were on insulin and the rest used different oral hypoglycemic agents. For the presence of other comorbid diseases, 35.8% had one and 4.7% had more than one comorbid disease.

*Table 1. Socio-demographic characteristics of the study population.*

| Characteristics | Total N=380 | Cognitive function | | |
| | | Dementia n=191 50.3% | Mild n=151 39.7% | Normal n=38 10% |
|---|---|---|---|---|
| Age Mean ± SD | 55.47 ± 8.35 | 55.95 | 54.99 | 54.95 |
| BMI Mean ± SD | 29.69 ± 5.04 | 29.54 | 29.97 | 29.37 |
| Duration of Diabetes Mean ± SD | 10.18 ± 7.66 | 10.11 | 10.18 | 10.54 |
| Duration of comorbid disease Mean ± SD | 10.47 ± 8.61 | 10.11 | 9.95 | 12.5 |
| HbA1c Mean ± SD | 8.68 ± 1.47 | 9.26 | 8.49 | 8.44 |
| Gender (%) Male Female | 54.7 45.3 | 98 93 | 86 65 | 24 14 |
| Marital status (%) Single Married | 1.3 98.7 | 2 189 | 3 148 | 0 38 |
| Educational level (%) Primary Secondary University | 58.4 28.2 13.4 | 143 38 10 | 71 56 24 | 8 13 17 |
| Employment (%) Not employed Employed | 73.4 26.6 | 156 35 | 106 45 | 17 21 |
| Monthly income (%) less than 500000 IQD 500000-1000000 IQD more than 1000000 IQD | 38.4 56.3 5.3 | 98 90 3 | 44 96 11 | 4 28 6 |
| Smoking (%) Yes No | 18.7 81.3 | 28 163 | 30 121 | 13 25 |
| Presence of other co-morbid disease (%) Yes No | 35.8 64.2 | 72 119 | 46 105 | 18 20 |
| More than one comorbid disease (%) Yes No | 4.7 95.3 | 9 182 | 6 145 | 3 35 |

**Cognitive patterns among study population:** The cognitive function was evaluated using the SLUMS examination which consists of 11 questions and a score range between 0-30. The mean score for the cognitive function examination was 19.23 ± 4.15 with a median value of 19. As more than half of the study population had a low educational level (primary 58.4%) the cutoff point used was ≤ 24. So, the result demonstrated that 90%had impaired cognitive function (Table 2). The Kolmogorov - Simonov test showed (P < 0.05) that indicated the nonnormal distribution of the results and non-parametric statistical tests (spearman's correlation) were used to examine the correlation between the SLUMS scores and socio-demographic characteristics of the T2D patients. No significant correlation between cognitive function and age, BMI, HbA1c, duration of diabetes, and duration of co-morbid disease. Significant correlation between cognitive function and RBS level (P < 0.05) (Table 3).

*Table 2. Percent and frequency of impaired and normal cognitive function among participants.*

| Variables | Primary and secondary | University | Frequency | Percent |
|---|---|---|---|---|
| Dementia | 181 | 10 | 191 | 50.3 |
| Mild | 127 | 24 | 151 | 39.7 |
| Normal | 21 | 17 | 38 | 10 |

*Table 3. The correlation between demographic characteristics and cognitive function (continuous).*

| Variables | N | Rho* | P value |
|---|---|---|---|
| Age | 380 | -0.005 | 0.333 |
| BMI | 380 | 0.012 | 0.808 |
| Diabetes duration | 380 | 0.012 | 0.813 |
| Duration of co-morbid disease | 136 | 0.018 | 0.835 |
| FBS | 318 | -0.024 | 0.666 |
| HbA1c | 380 | 0-0.081 | 0.113 |
| RBS | 64 | -0.307 | **0.014** |
| Number of cigarettes | 71 | 0.078 | 0.517 |
| * Spearman's correlation. | | | |

Non-parametric statistical tests (Mann-Whitney test for dichotomous data and Kruskal-Wallis test for polychromous data) were used to examine the differences in SLUMS scores among socio-demographic groups of the T2D patients. Significant differences were found between cognitive function and gender, smoking, educational level, employment, and monthly income. While no significant differences were found with the marital state. The differences between SLUMS scores and the type of medications used for diabetes also were examined and no significant differences were found (Table 4).

*Table 4. The differences between demographic characteristics and cognitive function (categorical).*

| Variables | Mean | Median | SD | P value |
|---|---|---|---|---|
| **Gender*** | | | | |
| Male | 19.72 | 20 | 3.85 | **0.024** |
| Female | 18.63 | 19 | 4.42 | |
| **Smoking*** | | | | |
| Yes | 20.34 | 21 | 3.97 | **0.015** |
| No | 18.97 | 19 | 4.16 | |
| **Marital state*** | | | | |
| Single | 19.4 | 20 | 2.96 | 0.993 |
| Married | 19.23 | 19 | 4.17 | |
| **Educational level**** | | | | |
| Primary | 17.85 | 18 | 4.13 | **<0.05** |
| Secondary | 20.57 | 21 | 3.32 | |
| University | 22.41 | 23 | 3.04 | |
| **Employment*** | | | | |
| Not employed | 18.59 | 19 | 4.23 | **<0.05** |
| Employed | 21 | 21 | 3.35 | |
| **Monthly income**** | | | | |
| Less than500000IQD | 17.31 | 17 | 4.29 | **<0.05** |
| 500000-1000000IQD | 20.23 | 20 | 3.61 | |
| More than1000000IQD | 22.5 | 22 | 2.58 | |
| **Insulin*** | | | | |
| Yes | 19.33 | 20 | 4.27 | 0.736 |
| No | 19.15 | 19 | 4.06 | |
| **Glibenclamide*** | | | | |
| Yes | 19.03 | 19 | 4.02 | 0.56 |
| No | 19.33 | 20 | 4.22 | |
| **Metformin*** | | | | |
| Yes | 19.08 | 19 | 4.15 | 0.309 |
| No | 19.52 | 20 | 4.15 | |
| **Glimepiride*** | | | | |
| Yes | 18.69 | 19 | 3.91 | 0.274 |
| No | 19.28 | 20 | 4.18 | |
| **Sitagliptin+ Metformin*** | | | | |
| Yes | 19.33 | 20 | 4.07 | 0.766 |
| No | 19.22 | 19 | 4.17 | |
| *Mann-Whitney U test, **Kruskal-Wallis test. | | | | |

**Discussion.**

This study was conducted to explain the relationship between DM and cognitive function, and to explain the associated factors. A number of studies confirmed this association and examine different risk factors for developing cognitive problems. Diabetes associated with both subtypes of MCI (aMCI and naMCI) in middle-aged patients [6]. One study found that DM was associated with a twofold increased risk of vascular dementia, 47% and39% increased risk of dementia and Alzheimer's dementia among elderly patients respectively and this association was independent of the cardiovascular comorbidities [15].

The prevalence of cognitive impairment in the population study was found (90%). Other studies found a different prevalence of cognitive impairment this may be due to different factors like the educational level of the study population and other Socio-demographic characteristics, and different screening tools and cut-off points. In Saudi 80%, Pakistan 24.4 % [16], China 28 % [17], and other regions 31.5 % [18], 21.8 % [19].

Diabetes is associated with a reduction in brain volume especially in certain region hippocampus, cerebellar area, and thalamus [20]. These structural changes occur prior to functional changes. There is controversial evidence about the

effect of glycemic control on cognitive function as some studies reported that tight glycemic control in midlife had a protective effect against the late-life decline in cognitive function [21]. On the other hand, the intensive glycemic control in the older population did not have a protective effect against the decline in cognitive function [22]. Although this may be due to the need of poly pharmacy to get this control and side effect associated with this medication, or the increase chance of hypoglycemia which also had a negative effect on cognitive function.

No significant correlation was found with age, duration of diabetes, and HbA1c level. While a significant association was found with post-prandial glucose level, gender, smoking, educational level, employment, and monthly income. This finding with regard to age, duration, and HbA1c level may be due to the lower age of the study population (mean 55.47 years) compare with another study conducted on elderly patients > 60 years old [9]. A study conducted on young adults (<60) found weak negative relation with HbA1c level, weak positive relation with duration of DM, and moderate positive relation with education [23]. Studies revealed that the HbA1c level did not reflect the same meaning as in young people. This may be due to the effect of comorbidity in the older population which had impaction on the life span of red blood cells. The HbA1c level tends to increase by 0.01 mmol/mol / year after 20 years old and the suggested formula to calculate the corrected HbA1c level. This information should be taken into consideration when deciding the target HbA1c in elderly diabetic patients to reduce the risk of hypoglycemia [24,25]. [corrected HbA1c (%) for age was 5.09+0.01 (age)]

A significant association with gender was observed in another study [26] this association is stronger in men, and aMCI was more common among females while naMCI was more common among male [6]. In spite of this, another study conducted in Cairo found that cognitive impairment was more prevalent among female [27-29]. This may be due to the stronger vascular adverse effect of diabetes in women than men [30]. The biological differences between male and female for example the endogenous estradiol in women may play a role in this effect [31]. Significant association with smoking was observed this in contrast to another study which reported no association [32]. The significant association with educational level was confirmed in another study [2]. Some studies also found that the effect of education is more profound than the effect of age on cognitive function [33]. Although another study found that age has a more pronounced effect on cognitive function than education [34]. Occupation and socioeconomic state also affect the cognitive function in diabetic patients [2]. Low socioeconomic state and low income were observed in another study this may be due to low dietary intake, low health care services, and social isolation [35]

No significant difference was found between cognitive function and medication used for diabetes this result obtains in another study [36]. Whereas other studies found that cognitive function impairment were more likely to develop in patients who were used insulin compared with patients on oral hypoglycemic agents [37,38]. Another study found an association with oral hypoglycemic agents [39].

## Conclusion.

Decline cognitive performance is common among diabetic patients, 90 % had a decline in cognitive function. It is associated with gender, smoking, educational level, employment, and monthly income. No association was reported with age, HbA1c, duration of diabetes, and medication used for diabetes.

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