



Mental state, psychoemotional status, quality of life and treatment compliance in patients with Type 2 diabetes mellitus

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Aim: To identify correlations between quality of life (QoL), emotional and mental state in patients with Type 2 diabetes mellitus (T2DM) and to evaluate its contribution in prediction of compliance. **Materials & methods:** The T2DM patients aged 18–75 years with at least 12 weeks of stable hypoglycemic therapy were included to this cross-sectional study. We used Mini Mental State Examination (MMSE) for mental state assessment, Hospital Anxiety and Depression Scale (HADS) for anxiety and depression level and EQ-5D for QoL. Compliance level was self-reported by patients. **Results:** The QoL positively correlates with MMSE score ($p < 0.0001$) and negatively with HADS anxiety ($p < 0.0001$) and depression ($p < 0.0001$) levels. The MMSE score is higher ($p < 0.0001$), and both HADS levels are lower ($p < 0.01$) in patients with higher compliance level. **Conclusion:** Cognitive function and psychoemotional state in T2DM patients are important for treatment compliance and QoL and are to be corrected whenever possible.

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Diabetes mellitus (DM) has a significant negative influence on all aspects of patients' life, which are mostly physical and behavioral limitations, as well as disease-related patterns of social interaction. The influence leads to changes in a patient's psychoemotional status, which, together with the mental status, is the significant component of formation of treatment compliance [1–3]; however, currently this aspect is not fully understood in the Russian population.

There is the correlation between the mental status and components of the psychoemotional status [4]. Patients with dementia have motivational disorders highly specific for the cohort [5,6]. Patients with diagnosed major depression have cognitive disorders such as impaired attention, short-term memory and managing (regulatory) functions – ability to suppress nonrelevant reactions and plan your actions; hereby, according to the common opinion, memory problems are secondary to the impaired attention [7]. The intensity of cognitive disorders in patients with depression correlates not only with the depression and grief affect levels, but also with manifestations of anxiety symptoms, primarily due to disorders of verbal memory and refocusing in patients with anxiety [8].

Psychoemotional and mental status influence not only patients' treatment compliance, but also their quality of life [8,9], an increase of which is one of the key treatment goals. Hereby, the risk of depressive conditions in DM patients is 1.5- to two-times higher than in the population, and depressive and anxiety disorders occur more than in 80% patients with Type 2 diabetes mellitus (T2DM) [10,11] among which there are more women than men [12]. Patients with DM have also the increased risk of cognitive disorders up to dementia due to metabolic and vascular damages of cerebral tissues [13].

The problem of the decreased efficacy in routine practice in comparison with the clinical study results associated with imperfect treatment compliance of patients, as well as the presence of complex relationships between the psychoemotional and mental status, quality of life and treatment compliance, warranted the present study with regards to specifics of the Russian population of patients with T2DM.

We have conducted this cross-sectional study to identify correlations between quality of life, emotional and mental status in patients with T2DM and to evaluate the contribution of patient's cognitive function and emotional status in prediction of compliance.

Materials & methods

Study design

It was the cross-sectional monocenter study to which patients with T2DM were included regardless of their result in the cognitive function assessment. All patients were included in the study in the period from April 2017 to April 2018, and patients completed the proposed set of questionnaires.

Eligibility criteria

Patients with verified diagnosis 'T2DM' of both sexes, aged 18–75 years, were included to the study. All patients should have taken hypoglycemic therapy in stable doses for at least 12 weeks prior to their study inclusion.

The patients were included to the study on the base of Almazov National Medical Research Centre (Saint Petersburg, Russia) when they referred to the center for examination and treatment in routine clinical practice. All patients signed the informed voluntary consent prior to the study inclusion. The present study was approved by the independent ethics committee.

The only exclusion criteria were inability to follow the study procedures because of any reason.

Outcome measures

During the present study, the patients completed the set of standardized questionnaires validated for Russia which consisted of mini mental state examination (MMSE), hospital anxiety and depression scale (HADS) and European quality of life questionnaire (EQ-5D). All patients also provided the information about their sex, race, age, education level, duration of diabetes, last known HbA1c level (in case the patient was aware of it), self-reported compliance (frequency of drug intake omission – 'omit several times a month', 'omit once a month or more rarely' and 'never omit') and history of hypoglycemic drug withdrawal ('yes' or 'no').

The MMSE is a widely used instrument for the assessment of cognitive functions both in clinical studies and routine practice. The scale is a simple and valid screening test used in patients of the somatic profile [14]. The recognized test limitation lies in its low sensitivity in diagnostics of early dementia stages [15], which is allowed in the present study as dementia diagnostics is not our aim. Other limitations of the MMSE use is the result dependence on a patient's age, education level and ethnic group [15], due to which the parameters were considered in planning and analysis of the study data. The scale consists of ten questions and allows comprehensive assessment of patient cognitive function (orientation in time and place, object registration, attention, calculation, recall of earlier registered objects, language perception and copying the image). The processing of questionnaire results is extremely simple and lies in addition of scores obtained by a patient for each completed questionnaire task, hereby maximum score 30 corresponds to the absence of cognitive disorders. Minimum possible score 0 corresponds to a full patient's incapacity to perform any components of proposed tasks.

Key components of patients' psychoemotional status may be assessed using the HADS with the sufficient sensitivity and specificity when used in clinical studies and general medical practice [16], hereby the depression subscale reflects primarily anhedonia manifestations (including – inability to cope with everyday tasks) and focuses on moderate depressive disorders excluding physical manifestations of the depressive condition and suicidal thoughts from the assessment [17], which was not the aim of the present study. The scale use implies a separate processing of anxiety (HADS-A) and depression (HADS-D) subscales via simple addition of scores; hereby, 0–7 scores in each of the scales correspond to the absence of significant anxiety or depression symptoms, 8–10 scores – subclinical symptoms and 11–21 scores – clinical anxiety or depression symptoms.

The European quality of life questionnaire (EuroQoL, EQ-5D) is one of the most widely used generic index measures of health-related quality of life [18], accompanied with the visual analog scale 0–100. The questionnaire is targeted mainly on a subjective health assessment by a patient per five main categories (mobility, self-care, usual activities, pain or discomfort, emotional conditions). Some investigators tell about its low sensitivity for a specific assessment of the quality of life, not quality of health in general [19], and nevertheless, the questionnaire meets the declared aim of the study exactly owing to its subjectivity, and is rather compact to be filled by patients with numerous somatic disorders and, presumably, the decrease of cognitive functions. The results are processed per the standardized method based on 243 possible weighted health conditions. The final EQ-5D index is the range from

0 (condition corresponding to death) to 1 (complete health), self-assessment of health condition per VAS – from 0 to 100, where 100 reflects complete health [20].

All above-mentioned questionnaires have been selected with regards to the fact that patients will complete them simultaneously. While selecting questionnaires and scales, the investigators tried to maintain the balance between the test sensitivity and specificity, and patients' ability to complete them fully without the decrease of attention and motivation during the completion. All three questionnaires are widely used both in clinical studies and routine clinical practice, and are validated for the use in the Russian population.

Primary end points

Primary end points in the study are selected as follows:

- Correlation between quality of life assessed per EQ-5D and MMSE, HADS-A and HADS-D scores;
- Correlation between self-reported compliance and MMSE, HADS-A и HADS-D scores.

Secondary end points

Secondary end points are selected as follows:

- Correlation between MMSE and HADS-A scores;
- Correlation between MMSE and HADS-D scores;
- Correlation between MMSE and HADS-A scores with HADS-D stratification.

Statistical methods

All data analyses were made using RStudio (R version 3.5.1 for Windows) software.

Primary end points were described as mean $\pm$ standard deviation. Secondary end points were analyzed with the use of ANOVA, providing testing for one dependent and several independent variables for each test. We provide the data, which are both adjusted and not adjusted for the age and education level, when correction is required (MMSE). The linear regression model is used to describe correlations between MMSE, HADS and EQ-5D scores. Mann–Whitney U-test was used for comparison of MMSE scores in patients with and without the history of hypoglycemic drugs withdrawal. Kruskal–Wallis test followed by Mann–Whitney U-tests and Bonferroni correction were used for comparison of three or more unmatched groups.

A p-value of < 0.05 was accepted to be statistically significant. Correlation coefficient (r) should be assessed in accordance with the Chaddock scale.

Ethics committee review

The research was approved by the V.A. Almazov National Medical Research Center local ethics committee.

Results

Baseline population characteristics

A total of 106 patients aged 57.6 ± 9.3 years were included in the study (41.5% – men). Diabetes duration was 9.6 ± 7.4 years. A total of 63 patients (59.4%) knew their level of glycated hemoglobin at the study entry, and it was $9.38 \pm 1.38\%$. Three patients (2.8%) had only completed secondary school education, 29 (27.4%) had tertiary education, 14 (13.2%) had uncompleted higher education, and 60 (56.6%) had completed higher education. A total of 62 patients (58.5%) stated that they had ever withdrawn the hypoglycemic therapy prescribed by the physician on their own, and nowadays, 29 of them (27.4%) omit the drug intake several times a month, 36 (34.0 %) once a month or more rarely, and 41 (38.6%) stated that they had never omitted the drug therapy. The description of the results obtained with the use of EQ-5D, MMSE and HADS scales are provided in [Table 1](#).

Primary end points

The investigation of the relationship between the quality of life and patients' psychoemotional status showed the strongest correlation between EQ-5D and MMSE scores, to a smaller extent – between HADS-A and HADS-D scores. The obtained results do not depend on the assessment method for the quality of life (per the questionnaire or VAS). The statistic description of the correlations identified between EQ-5D scores and MMSE, HADS-A, and HADS-D scores is provided in [Table 2](#).

Table 1. Mini mental state examination, hospital anxiety and depression scale and EQ-5D scores of the study patients.

Test/ scale	Mean $\pm$ standard deviation	Median	Min	Max
MMSE	25.4 $\pm$ 2.3	26.0	20.0	30.0
HADS-A	8.8 $\pm$ 4.0	8.5	0.0	19.0
HADS-D	6.5 $\pm$ 3.4	6.0	0.0	15.0
EQ-5D index	0.700 $\pm$ 0.100	0.679	0.555	1.000
EQ-5D, VAS	56.0 $\pm$ 14.8	57.5	30.0	95.0

MMSE: Mini mental state examination; HADS: Hospital anxiety and depression scale.

Table 2. Linear regression model coefficients for correlations between EQ-5D and mini mental state examination, hospital anxiety and depression scale-A and hospital anxiety and depression scale-D scores in Type 2 diabetes mellitus patients.

	EQ-5D index			EQ-5D VAS		
	B $\pm$ SE (B)	p-value	r	B $\pm$ SE (B)	p-value	r
MMSE	0.042 $\pm$ 0.005	<0.0001	0.66	4.730 $\pm$ 0.416	<0.0001	0.74
HADS-A	-0.024 $\pm$ 0.004	<0.0001	-0.54	-2.007 $\pm$ 0.383	<0.0001	-0.46
HADS-D	-0.020 $\pm$ 0.003	<0.0001	-0.53	-1.980 $\pm$ 0.304	<0.0001	-0.54

MMSE: Mini mental state examination HADS: Hospital anxiety and depression scale.

Table 3. Self-reported compliance and mini mental state examination, hospital anxiety and depression Scale-A and hospital anxiety and depression scale-D scores in Type 2 diabetes mellitus patients.

	Self-reported compliance			p-value [†]
	'Omit several times a month'	'Omit once a month or more rarely'	'Never omit'	
MMSE	23.74 $\pm$ 1.93	25.11 $\pm$ 1.01 [‡]	26.90 $\pm$ 1.88 ^{‡,§}	<0.0001
HADS-A	8.00 $\pm$ 3.35	6.69 $\pm$ 2.96	5.39 $\pm$ 3.47 [‡]	0.002
HADS-D	11.04 $\pm$ 4.64	8.75 $\pm$ 3.40 [‡]	7.12 $\pm$ 3.40 [‡]	<0.0001

Remark:

[†] Kruskal–Wallis test.[‡] p < 0.05 (Mann–Whitney U-test, Bonferroni correction) compared with 'omit several times a month'.[§] p < 0.05 (Mann–Whitney U-test, Bonferroni correction) compared with 'omit once a month or more rarely'.

MMSE: Mini mental state examination HADS: Hospital anxiety and depression scale.

As for feasibility to routine clinical practice, we should state the correlation not only between the levels of the cognitive deficit and of grief affect, and a patient's quality of life, but also his/her treatment compliance. The higher was the frequency of omissions in hypoglycemic therapy, the lower MMSE score had the patient ($p < 0.0001$). As well, self-reported compliance was lower in patients with higher HADS-D ($p < 0.0001$) and HADS-A scores ($p = 0.002$). Mean $\pm$ standard deviation scale scores are presented in Table 3.

Hereby, the patients' treatment compliance correlates positively to their quality of life both when assessed with EQ-5D index ($p < 0.0001$; $r = 0.50$), and when the quality of life is assessed per VAS ($p < 0.0001$; $r = 0.45$).

Another indirect method for the assessment of treatment compliance is the assessment of medical history of the drug withdrawal by a patient on his/her own. In this case, the above-mentioned scales may also serve as the predictive factor. The patients that had ever withdrawn the hypoglycemic therapy on their own, in comparison with the patients denying the spontaneous withdrawal, had the lower MMSE score (24.79 ± 2.31 and 26.07 ± 1.86 , correspondingly, $p < 0.0001$), and higher HADS-A scores (7.10 ± 3.47 and 5.68 ± 3.12 , correspondingly, $p = 0.005$) and HADS-D (9.48 ± 3.89 and 8.12 ± 3.89 , correspondingly, $p = 0.002$).

Secondary end points

Both anxiety and depression levels determined per HADS scale, correlated negatively with the patients' cognitive function in the present study ($p < 0.0001$ for both parameters), and the power of the correlation between MMSE scores and depression subscale scores ($r = -0.54$) was higher than the one between MMSE scores and anxiety subscale scores ($r = -0.43$). The factors of depression and anxiety levels remained significant when MMSE score

Table 4. Linear regression model coefficients for correlations between mini mental state examination and anxiety and depression level of Type 2 diabetes mellitus patients.

	Unadjusted			Adjusted		
	B ± SE (B)	p-value	r	B ± SE (B)	p-value	R ²
HADS-D	-0.312 ± 0.048	<0.0001	-0.54	-0.244 ± 0.047	<0.0001	0.41
Age	–	–	–	-0.089 ± 0.020	<0.0001	
Education	–	–	–	0.145 ± 0.192	0.452	
HADS-A	- 0.300 ± 0.061	<0.0001	- 0.43	-0.289 ± 0.052	<0.0001	0.43
Age	–	–	–	-0.119 ± 0.019	<0.0001	
Education	–	–	–	0.174 ± 0.188	0.359	

HADS: Hospital anxiety and depression scale.

was determined, as well as after correction for the patients' age and education level. The description of the linear regression models coefficients for correlations between MMSE and HADS subscales is presented in Table 4.

Additionally, the analysis of the relationship between MMSE and HADS-A scores depending on HADS-D score was made. In accordance with the adopted clinical interpretation of the results, the cutoff equals to seven scores was selected (0–7 scores corresponding to the absence of significant symptoms). The correlation was significant in the group with HADS-D ≥ 8 scores ($p = 0.0008$), but not in the group with HADS-D ≤ 7 ($p = 0.475$).

Discussion & recommendations

In the present study, the correlations between the cognitive and psychoemotional status of patients with T2DM, their quality of life and treatment compliance were determined. Despite the fact that the cross-sectional study design by its essence does not allow us to make the conclusion on the trends in the identified correlations, there are grounds to assume that cognitive and psychoemotional disorders reduce patients' quality of life significantly. Johari *et al.* [21] showed the impact of the cognitive status (assessed with Montreal Cognitive Assessment Scale) of elderly patients with T2DM on social relations and environmental domains of the quality of life assessed with the use of WHO Quality of Life-BREF-short version questionnaire. In this work, the correlation of depression level was shown (assessed with the use of the geriatric depression scale) both in psychological and physical health domains [21]. Other works are devoted primarily to the negative impact of depression on quality of life of patients with DM [22,23], as the contribution of the cognitive status to patients' quality of life remains not much known and is presented conclusively only in individual works [9]. In our work, the power of the correlation between the quality of life and cognitive deficit appeared to be higher than the one between the quality of life and components of the psychoemotional status which underlines once again the importance of assessment of patients' cognitive status.

The cognitive and psychoemotional status in our study also correlated with the patients' treatment compliance both based on the regular therapy and adherence to physician's prescriptions. Our conclusions are confirmed in the studies on various nosologies: diagnosed depression is associated with the decreased compliance in Parkinson's disease [24], memory disorder – in Alzheimer's disease [25], and the general assessment of the cognitive function influences significantly the outcomes of the postoperative period in bariatric surgery [26,27] and administration of antihypertensive drugs [28]. The total data proves the generality of the conclusions. The use of MMSE and HADS in routine clinical practice allows to clarify the prediction of patients' treatment compliance based on patient's characteristics to a larger extent rather than drug characteristics (in this case, the main factors of noncompliance nowadays are treatment cost, adverse events and dosing regime – factors which are scarcely influenced by an attending physician).

The trend in the correlation between cognitive deficit and changes of the psychoemotional status are significantly more debated. The fact of cognitive deficit being due to chronic metabolic and vascular disorders is well known in patients with DM [29,30]; however, it may be scarcely determined unanimously which disorder is the primary one. Vascular and metabolic brain disorders may lead to atherosclerotic endogenous depression (ICD: F32, F33) [31], and the symptoms describing the decrease of cognitive functions, will correspond to the complaints common for patients with depression on the decreased working capacity, attention concentration, increased fatigue, but affective symptoms typical for depressive conditions will be evened significantly [32]. Meanwhile, the disease itself is associated with the risk of a depressive condition [11], including the one due to a significant number of limitations in everyday activity and stress factors determined by the presence of DM. In this case, retardation of mental processes and,

consequently, the decrease of cognitive function will be the clinical manifestation of depression [33], and cognitive disorders assessed per MMSE, will be secondary to aggravation of the depressive affect assessed per HADS-D scale. Nevertheless, the presence of the correlation between the cognitive function and depression level in patients does not cause any doubts, and as it has been shown in the present study, does not depend either on the patients' age or education level (main factors influencing the result of MMSE use).

In our study, the significant negative correlation was also shown between MMSE score and patients' anxiety level assessed per HADS-A scale. The relationship is most likely due to the decrease of attention and verbal memory [34], which are assessed within MMSE. Moreover, the phenomenon of narrowing attention on potentially hazardous stimuli in anxiety condition is well known [8] which results in worsened results in all the cognitive tests that require patient's attention to be made (attention and calculation domain of MMSE). It is of interest that the correlation between the cognitive function and anxiety level was significant only in patients with HADS-D ≥ 8 of 21 scores, which corresponds to the presence of subclinical or clinical manifestations of the depressive syndrome. The obtained results warrant the complex assessment of a patient's psychoemotional status.

Future perspective

We have shown that HADS (for assessment of anxiety and depression levels) and MMSE (for assessment of a patient's cognitive status) scales may be used in routine practice to predict a patient's treatment compliance. The presence of correlations between HADS scores and patient's quality of life shows the important role of the psychoemotional component in achievement of the patient-oriented goal of DM treatment, and namely, the increase of quality of life. The presence of correlations between the cognitive function and patient's psychoemotional status does not cause doubts; however, the trend in correlations may not be currently determined unanimously which shows the necessity of the complex approach to the management of the impaired functions. The retardation of the decreased cognitive function and correction of depressive and anxiety affect in patients with DM are important treatment components for patients' treatment compliance and increase of their health-related and general quality of life.

Study limitations

(1) Cross-sectional study design does not allow to assess the trend in the identified correlations; however, we have tried to explain logically our concepts on possible causalities in section 'discussion'.

(2) Patients with MMSE 20 scores and above were included to the study (mild dementia, predementia disorders, absence of cognitive deficit), so the conclusions might be not valid for patients with moderate and severe dementia. However, we did not select patients especially per the end point and may assume that most patients with T2DM have MMSE at least 20 scores.

The compliance data have been collected as the patient-reported data and are categorical rather than quantitative which reduces the end point sensitivity to some extent, but the correlations shown do not cause any doubts.

Summary points

- Diabetes mellitus (DM) affects all aspects of patients' lives, including psychoemotional and mental state and quality of life.
- These parameters seem to be a key to the treatment compliance and, consequently, on the effectiveness of hypoglycemic drugs.
- Quality of life score positively correlates with mental state score (measured with mini mental state examination [MMSE]) – the better cognition a DM patient has, the better his/her quality of life is.
- Quality of life score correlates negatively with both anxiety and depression levels (measured with hospital anxiety and depression scale [HADS]) – these statistical findings prove our experience-based assumptions.
- The MMSE score is higher and HADS-A and HADS-D are lower in patients with higher self-reported compliance.
- The negative correlation between both HADS-scales and MMSE is observed even after applied adjustment (patient's age and education level).
- Statistically proven suggested interrelationships between psychoemotional and mental state, quality of life and compliance in Type 2 DM patients highlight the need of paying special attention to these conditions beyond exceptionally clinical considerations.

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Data sharing statement

The authors certify that this manuscript reports original clinical trial data. Individual data will not be available unless it is personally required, in which case the principal investigator should be contacted.

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