ETHIOPIAN INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY RESEARCH

eISSN: 2349-5715 pISSN: 2349-5707

Volume: 12, Issue 02, February-2025 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980 2024: 7,662

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QUALITY OF LIFE AND COGNITIVE FUNCTIONS IN PRIMARY HYPOTHYROIDISM

Relevance: Currently, hypothyroidism is one of the most common forms of endocrine pathology. The prevalence of manifest hypothyroidism is 0.2 - 2%, subclinical - 10% [4, 5]. The relevance of the problem of hypothyroidism in the clinical practice of doctors of various specialties is due to the fact that with a deficiency of thyroid hormones, severe disorders develop in all organs and systems without exception. The multiple organicity of the lesion includes the problems of thyroidology in the sphere of interests of representatives of various disciplines. This fully applies to the effect of hypothyroidism on the mental and neurological status of patients [6, 7].

The most studied hypothyroid disorders in this regard are neuromuscular disorders (hypothyroid myopathy and myotonic phenomenon) and peripheral nerve damage, the prevalence of which is very variable. Vestibulocerebellar disorders and, less frequently, extrapyramidal disorders are mentioned among the signs of organic brain damage. In the structure of chronic encephalopathy in hypothyroidism, psychoemotional and intellectual disorders are most often described (7, 9).

The polymorphism of the clinical picture of damage to the psyche of patients with hypothyroidism has been described by domestic and foreign authors, including the fundamental works of V.G. Baranov (1966) and I.D. Levit (1977), as well as A.K. Dobrzhanskaya (1973), B.V. Drivotinov and M.Z. Klebanov (1989), A.P. Kalinin and S.V. Kotov (2009).

However, there is still no consensus on the features of quality of life in patients with hypothyroidism. Health-related quality of life assessment has become a mandatory attribute of modern research. It allows you to determine the impact of a disease or a disorder on the state of a patient's key functions, the actual effectiveness of therapy and rehabilitation programs, and predict the course and outcome of the disease. All of the above shows the relevance of the problem and the expediency of studying it in the clinic.

The purpose of the study. To determine the quality of life in patients with primary hypothyroidism, depending on gender, using standardized indicators of the SF-36 questionnaire scales.

Research material. 50 patients with primary hypothyroidism aged 18 to 59 years were examined, with an average age of 38.2+7.6 years. Patients of the Department of Endocrinology and Neurology of the Andijan State Medical Institute were taken under observation. The patients were observed in the departments of endocrinology and neurology of ASMI. The cause of primary hypothyroidism in all patients was autoimmune thyroiditis. All patients signed an informed consent to participate in the study.

Patients with psychiatric and severe somatic and thyroid diseases accompanied by a history of thyrotoxicosis syndrome, menopausal syndrome requiring hormone replacement therapy with estrogens, diabetes mellitus, autoimmune poly endocrine syndrome, pregnant and lactating women were excluded from the study.

Depending on the gender, the patients were divided into 2 groups. The first group included 30 (60%) female patients, and the second group included 20 (40%) male patients. Each group was

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divided into 2 subgroups depending on the form of primary hypothyroidism. Subgroup "A" - 35 consisted of patients with a manifest form of hypothyroidism, subgroup "B"- 15 consisted of patients with a subclinical form of hypothyroidism. The "A" subgroup of group I included 20 (66.7%) patients, the "A" subgroup of group II – 15 (75%). The "B" subgroup of group I included 10 (33.3%) patients, the "B" subgroup of group II – 5 (25%). The control group consisted of 20 healthy individuals, comparable to the main groups by gender and age.

All patients underwent a standard clinical and neurological examination (analysis of patient complaints, life history and medical history, objective examination, including the study of neurological status) and somatic examination.

The Short Mental Status Assessment Scale (MMSE) was used to objectify cognitive impairments. A maximum of 30 points, which corresponds to the optimal state of cognitive functions. The lower the final score, the more pronounced the cognitive deficit. According to the set of tasks, MMSE means superiority over other tests and requires more time to conduct, experts estimate the rather low sensitivity of the test. Also, for neuropsychological testing, a technique was used using a short scale-a battery of tests of frontal dysfunction. (Frontal Assessment Battery (FAB). In the diagnosis of dementia with a predominant lesion of the frontal lobes, it is important to compare the results of FAB. Frontal dementia is indicated by an extremely low FAB score (less than 11 points). The association of cognitive impairment with vascular factors was established using the Khachinsky scale, with scores of 7 and above (an average of 12-14 points) [2, 3]. The study of the quality of life of patients with primary hypothyroidism was conducted using the SF-36 General Health Questionnaire. The questionnaire was filled out by the patient independently or by interviewing the patient with a written record of his answers in the questionnaire form. The quality of life of patients was assessed in points (1).

Statistical processing and visualization of the obtained results were carried out using the software package for statistical analysis STATISTICA v. 10 and the built-in functions of the Microsoft Office Excel package. During the statistical analysis, the critical significance level of the null statistical hypothesis was assumed to be 0.05.

The results of the study. It should be noted that with manifest hypothyroidism in each group, the percentage of detection of comorbid pathology was higher. Cerebrovascular pathology and metabolic syndrome in women with manifest hypothyroidism were detected in 30.6% and 36.1% of cases, respectively.

The psychological history of the subjects was assessed as part of this project. The indicators of the subjects were compared with those of the control group. In patients with manifest hypothyroidism, MMSE and FAB cognitive function scores were significantly lower – 28.0 (27.0-29.0) points and 17.0 (16.0-18.0) points than in the control group – 29.5 (28.0-30.0) points (p=0.006) and 18.0 (17.0-18.0) points (p=0.022). In patients with hypothyroidism, cognitive impairment was estimated at 70.5% according to MMSE and FAB data.

Neuropsychological testing with assessment of memory, attention, and thinking function revealed signs of cognitive impairment in group I patients with high MMSE and FAB scores, which were among the leading (72.5%) in the structure of NS lesions in hypothyroidism. In patients with hypothyroidism, the proportion of mild cognitive impairment was 46.8%, moderate cognitive impairment was 30.6%, and cognitive impairment was not detected in 22.5% of cases.

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In patients of group II, the proportion of mild cognitive impairment was 39.5%, which is significantly lower than in the same group I ($p<0.005$). The percentage of moderate cognitive impairment was 18.4%, and 42.1% of cases of cognitive impairment were not detected (vol.4.6). compared with group I, and in group I, patients with moderate cognitive impairment prevailed over patients with moderate cognitive impairment in group II – 42.1% versus 12.3% (% calculation was made from the total number of patients within each group).

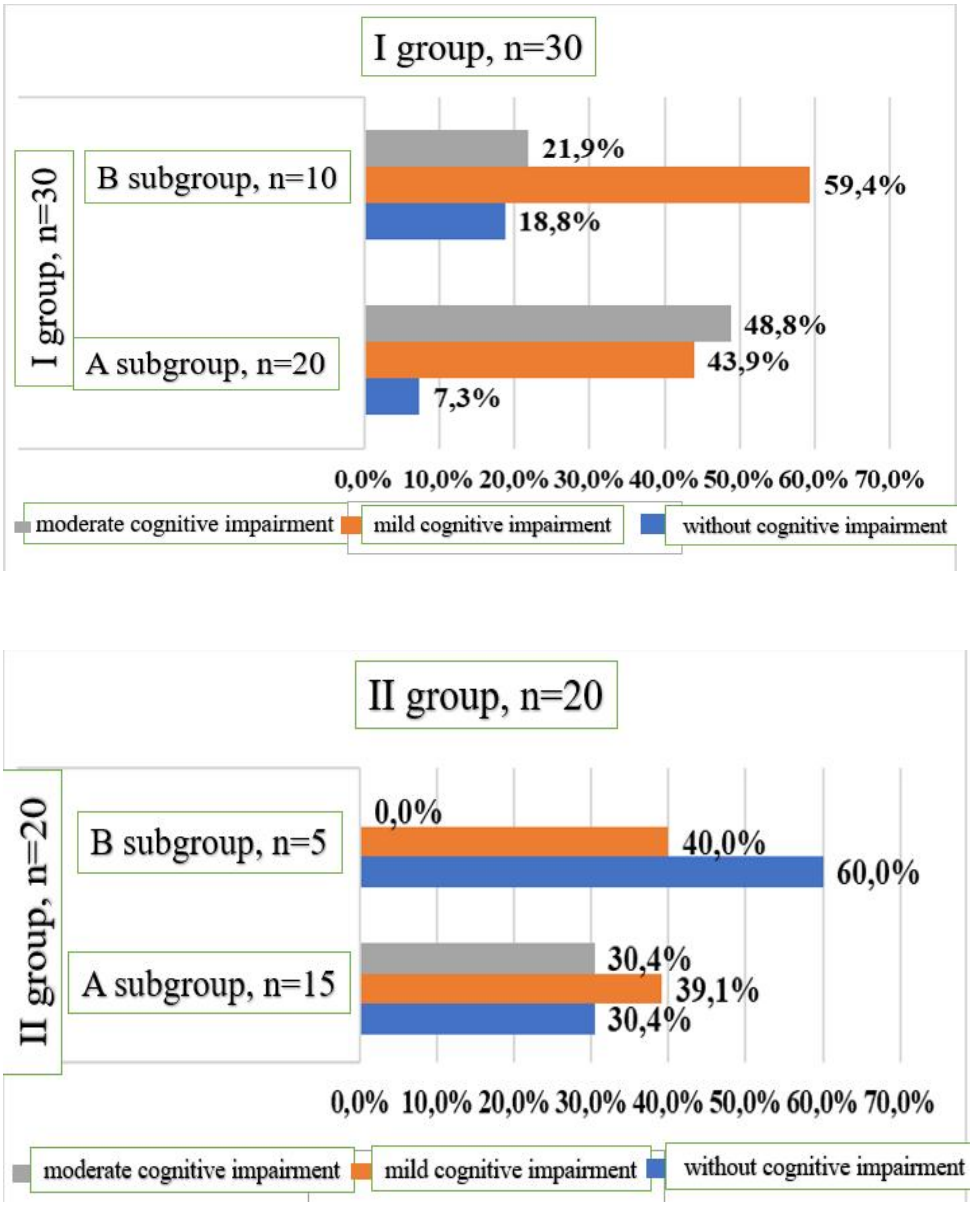

Figure 1. The structure of cognitive impairments in patients depending on the form of hypothyroidism and gender.

Regarding the identification of the degree of cognitive impairment in patients in subgroups, it can be said that patients with subclinical hypothyroidism in both groups had a higher percentage of patients without cognitive impairment (Fig.1). With manifest hypothyroidism in both groups, patients with moderate cognitive impairment and mild cognitive impairment were significantly more common

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(48.8%, 43.9%, 30.4%, and 39.1%, respectively). Figure 1 shows that with subclinical hypothyroidism, both groups had a higher percentage of patients without cognitive impairment.

In patients with manifest hypothyroidism, 40.4% had short–term memory disorders, 44.2% had memory productivity disorders, 84.6% had a decrease in the rate of memorization, and 25.9% had long–term memory disorders. In terms of short-term memory, patients with manifest hypothyroidism without cognitive impairment, with mild cognitive impairment and moderate cognitive impairment differed significantly from each other ($p<0.001$) and the comparison group ($p=0.001$). Memory productivity decreased mainly in patients with moderate cognitive impairment ($p<0.05$), delayed reproduction – in patients with mild cognitive impairment and moderate cognitive impairment ($p<0.05$). The increase in the severity of cognitive impairment on the background of decompensation of hypothyroidism was 45.2%; 45.2%; 9.6% without cognitive impairment mild cognitive impairment moderate cognitive impairment is associated with impaired long-term memory and memory productivity, since in patients with moderate cognitive impairment with increased TSH levels, the number of words reproduced by the fifth presentation ($rs=-0.69$; $p=0.020$) and delayed playback ($rs=-0.90$; $p<0.001$), decreased.

Attention disorders were found in 71.2% of patients with manifest hypothyroidism. Decreased concentration of attention was found in 29.8%, increased instability and attenuation in 47.1%. In 1.9% of cases, there were signs of attention rigidity, in 22.1% – an extremely fast pace of work. Decreased accuracy and concentration of attention prevailed in patients with mild cognitive impairment ($p<0.001$); decreased stability of attention in the first ($p=0.003$) and second ($p=0.002$) minutes, increased sample execution time ($p<0.001$) – in patients with moderate cognitive impairment.

Impaired thinking function in patients with manifest hypothyroidism was found in 52.9% and was characterized by slowness of mental activity (29.1%) with elements of specific situational thinking (40.0%), accelerated (3.6%) or rigid (23.7%) types of thinking with mild cognitive impairment and moderate cognitive impairment, disorders of analytical and synthetic function (3.6%) – with moderate cognitive impairment.

Patients with manifest hypothyroidism showed clinical signs of anxiety (43.2%) and depression (20.2%) and their subclinical manifestations (24.0 and 26.9%). With decompensation of hypothyroidism, patients with moderate cognitive impairment had a higher level of anxiety than patients without cognitive impairment ($p=0.040$), and the level of depression significantly differed from patients with mild cognitive impairment ($p=0.020$), without cognitive impairment ($p=0.030$) and the comparison group ($p=0.020$).

Patients with manifest hypothyroidism had a lower indicator on the Khachinsky scale – 3.0 (2.0-5.0) points than in the comparison group – 4.5 (3.0-6.0) points ($p=0.006$). The indicator on the Khachinsky scale of 4 points or less was registered in hypothyroidism at 74.0%, 7 points or more – at 2.9%. The total score from 5.0 to 6.0 on the Khachinsky scale was found to be 23.1%, indicating the contribution of cerebrovascular pathology to the development of cognitive impairment in hypothyroidism.

The contribution of the identified cognitive impairments to the clinical manifestations of cognitive impairment in hypothyroidism was assessed. The analysis group included cognitive impairments for which a statistically significant association was established with the identified cognitive deficits: thinking disorders ($\chi2=26.87$; $p<0.001$), disorders of short-term ($\chi2=56.83$; $p<0.001$) and long-term ($\chi2=30.85$; $p<0.001$) memory, changes in productivity ($\chi2=17.83$; $p<0.001$) and

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memorization rate ($\chi 2$=20.36; p<0.001), impaired concentration ($\chi 2$=38.18; p<0.001). Since there is no established relationship between the identified cognitive impairment, changes in psych emotional status (p=0.508; p=0.213) and attention stability (p=0.288), these parameters were not included in the construction of the logistic regression model. According to the results of the analysis, cognitive impairments were identified that made the greatest contribution to the clinical manifestations of cognitive impairment in patients with hypothyroidism: short-term memory (p<0.001), concentration (p=0.001) and long-term memory (p=0.028).

Changes in the cognitive status of patients with manifest hypothyroidism had a wave—like character of improvement — deterioration - improvement with an increase in positive dynamics, which later consolidated and became stable. Considering that the process of information transition from short-term memory to long-term memory is accompanied by functional and structural changes supported by the acetyl cholinergic system, it can be assumed that neuroprotective therapy with Cortexin has a direct neurotrophic, neurometabolic effect on cells and mediators of the central nervous system, as well as an effect on visual memory, which can be associated with improved connections of the frontal cortex.-parietal lobes with subcortical structures [6].

A study was also conducted on the quality of life in patients of the main study groups using standardized indicators of the SF-36 General Health Questionnaire scales.

According to most scales of the SF-36 questionnaire, lower values of quality of life indicators were noted in group I compared with quality of life indicators in group II, differences in quality of life indicators were statistically significant, with the exception of indicators of the scales "physical functioning" and "general health". Patients in the age groups had no statistically significant differences in standardized indicators of quality of life on all scales of the SF-36 questionnaire.

The table shows standardized indicators of quality of life according to the 8 scales of the SF-36 questionnaire in patients of the main study groups (with mild cognitive impairment and moderate cognitive impairment syndrome) in the groups. A statistically significant difference was revealed between the indicators of quality of life in Group I: indicators on the scale of "physical functioning" and on the scale of "vitality" were lower in patients with moderate cognitive impairment syndrome (U=22.5, p=0.032 and U=16, p=0.009). According to the other scales of the SF-36 questionnaire in group II and on all scales in group I, the quality of life indicators had no statistically significant differences between the main groups of patients studied.

Table

Standardized indicators of the quality of life of the SF-36 questionnaire scales (M±δ) in patients with primary hypothyroidism

SF-36 - Medical Outcomes Study Questionnaire Short Form	I group	II group
Physical functioning	42,6±9,5	54,1±8,3
Physical role functioning	37,2±8,1	40,8±7,2
Bodily pain	36,4±6,7	54,9±6,8

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General health perceptions	47,2±7,6	49,1±6,3
Social role functioning	38,5±5,3	54,2±4,6
Emotional role functioning	47,2±4,6	63,4±4,7
Mental health	40,5±6,1	60,2±5,8

According to our study, the quality of life of patients with primary hypothyroidism was influenced by the profile of moderate cognitive impairment. In patients with moderate cognitive impairment syndrome, there was a decrease in quality of life on the scale of "psychological health" (W=698.5, p=0.024), in patients with impaired dynamic practice – on the scale of "physical functioning" (W=325, p=0.003), in patients with impaired executive function – on the scale of "mental health" (W=698.5, p=0.024), in patients with impaired dynamic practice - on the scale of "physical functioning" (W=325, p=0.003), in patients with impaired executive function - on the scale of the scale "general state of health" (W=673.5, p=0.024). Impairments in other cognitive areas did not have a significant impact on the quality of life according to the SF-36 questionnaire scales.

The quality of life indicators of the SF-36 questionnaire scales in patients with primary hypothyroidism were influenced by emotional and affective disorders. In patients with asthenic disorder, quality of life indicators were reduced on all scales of the SF-36 questionnaire. In patients with depression, quality of life indicators were reduced on all scales of the SF-36 questionnaire, with the exception of the "pain" scale (K=4.7, p=0.095). The quality of life indicators in patients with increased situational anxiety were reduced on all scales of the SF-36 questionnaire, with the exception of the "role-based physical functioning" scale (K=5.52, p=0.063). Increased personal anxiety affected the quality of life indicators only on those scales that assess the mental component of health, on the scales of "physical functioning", "role-playing physical functioning", "pain" and "general health", the quality of life indicators did not significantly change (K=2.16, p=0.339; K=3.19, p=0.203; K=2.81, p=0.246; K=2.41, p=0.299, respectively).

Conclusions. The quality of life of patients with primary hypothyroidism is influenced by the profile of cognitive disorders. Disorders of the "executive" function, including dynamic practice, had a significant impact on the quality of life of patients with primary hypothyroidism and moderate cognitive impairment syndrome. Patients with moderate cognitive impairment syndrome who, according to the results of neuropsychological testing, had impaired "executive" function had lower quality of life on the "general health" scale, which characterizes physical health, disease resistance and prospects for treatment, assessed by the patient himself. Praxis is the ability to acquire and use a variety of motor skills, memorized and automated sequences of movements. The decrease in the quality of life indicator on the scale of "physical functioning" in violation of praxis confirms the direct relationship of regulatory cognitive insufficiency to self-care and daily physical activity of patients. In patients with primary hypothyroidism and moderate cognitive impairment, attention deficit hyperactivity disorder correlated with a lower score on the SF-36 "psychological health" scale. This meant that patients with moderate cognitive impairment and attention deficit disorder had anxiety and depressive states that determined the psychological distress of these patients.

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eISSN: 2349-5715 pISSN: 2349-5707

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