seem to be low in both countries, supporting the notion that thalassemias are not a major health problem there.

Keywords: alpha- and beta-globin mutations, thalassemias.

РЕЗЮМЕ

МУТАЦИИ ГЕНОВ АЛЬФА- И БЕТА-ГЛОБИНОВ В ГРУЗИИ И АРМЕНИИ

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Грузия и Армения расположены на северном краю пояса талассемии и граничат со странами с высокой распространенностью талассемии.

Целью исследования явилось установление частоты и потенциального спектра мутаций альфа- и бета-глобинов в Грузии и Армении.

Обследованы 202 и 190 субъектов. Обнаружены четыре мутации альфа-глобина (-3.7del, -4.2del, трипликация анти-3.7, поли-A2) у 9 (4,74%) армян и 4 (1,78%) грузин. Гетерозиготная мутация кодона 8 [-AA] бета-глобина выявлена только у одного жителя Армении. Частота распространения талассемии в обеих странах является низкой, подтверждая, что в этих странах талассемия не является ведущей проблемой здравоохранения.

რეზიუმე

ალფა- და ბეტა-გლობინის მუტაციები საქართველოსა და სომხეთში

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საქართველო და სომხეთი თალასემიის სარტყლის ჩრდილოეთ კიდეზე მდებარეობენ და ესაზღვრებიან იმ ქვეყნებს, სადაც თალასემიის მაღალი გავრცელება აღინიშნება.

კვლევის მიზანს წარმოადგენდა ალფა და ბეტა-გლობინის მუტაციების სიხშირისა და პოტენციური სპექტრის დადგენა საქართველოსა და სომხეთში.

გამოკვლეული იყო 202 და 190 სუბიექტი. აღმოჩნდა ალფა-გლობინის ოთხი მუტაცია (-3.7del, -4.2del, anti-3.7 ტრიპლიკაცია, poly-A2) 9 (4.74%) სომეხსა და 4 (1.78%) ქართველში. ჰეტეროზიგოტური ბეტა-გლობინის კოდონ 8 [-AA] მუტაცია გამოვლინდა მხოლოდ ერთ ინდივიდში სომხეთში. საერთო ჯამში, მტარებლების სიხშირე საქართველოსა და სომხეთში დაბალია, რაც მიუთითებს, რომ თალასემია ამ ქვეყნებში ჯანდაცვის სამსახურის წამყვან პრობლემას არ წარმოადგენს.

EVALUATION OF COGNITIVE IMPAIRMENT IN PATIENTS WITH MULTIPLE SCLEROSIS USING GEORGIAN LANGUAGE MONTREAL COGNITIVE ASSESSMENT

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Multiple sclerosis (MS) is a chronic inflammatory demyelinating and degenerative disease of the central nervous system (CNS). It usually develops between the ages of 20 and 40 years and is the leading cause of non-traumatic physical disability in young adults [5]. The clinical picture of MS is diverse and reflects the localization and extent of CNS lesions [16]. First clinical presentation of MS is known as clinically isolated syndrome (CIS). The most common form of MS is relapsing remitting multiple sclerosis (RRMS), characterized by alternating periods of relapse and remission. Eventually, many patients with RRMS deteriorate gradually and transition to secondary progressive MS (SPMS). It is estimated that about 15% of patients develop primary progressive MS (PPMS), characterized by worsening neurologic function from the onset of disease [16].

Over the past few decades, cognitive impairment (CI) has been recognized as an important feature of the disease. According to

various prevalence studies, CI affects 22%-70% of patients with MS [9,14]. Although it is more frequent and pronounced in progressive forms of MS, CI can occur in patients with clinically and radiologically isolated syndromes [1]. Majority of patients develop mild to moderate CI. Dementia due to MS is infrequent and has been reported in up to 15% of patients [17]. The neuropsychological aspects of CI in MS are quite specific. Some cognitive domains are most commonly and severely affected, while others remain intact. Information processing speed (IPS), verbal memory, visuospatial abilities, verbal fluency, and executive system are the most frequently impaired cognitive spheres [3]. Considering the unique clinical phenotype, application of standardized neuropsychological tools is advised for the screening and evaluation of cognitive deficits in MS patients [12].

Montreal Cognitive Assessment (MoCA) is a well-known screening test for MCI [13]. This test evaluates cognitive domains such as executive function, visuospatial ability, attention/concentration, language, verbal fluency, abstract thinking, delayed recall memory, and orientation. It has been translated and validated in many languages, including Georgian. The sensitivity and specificity of the MoCA test has been evaluated in many neurological disorders, including MS [18]. One of the main advantages of MoCA over other screening tests indicated for MS is that it evaluates the executive function [2].

The purpose of our study was to evaluate the prevalence and risk-factors of CI in patients with MS using the Georgian language Montreal Cognitive Assessment.

Material and methods. The study was conducted at S. Kechinashvili University Hospital from March 1, 2019, to March 1, 2020. The study protocol and informed consent form were approved by the ethics committee of Tbilisi State Medical University. Patients with MS who were admitted to the hospital were offered to enroll in our study. Finally, 53 individuals agreed to participate. All subjects signed the informed consent form prior to enrollment. Patients were recruited in accordance with the following inclusion criteria:

1. Willingness and ability to provide informed consent; 2. Confirmed diagnosis of MS according to McDonald criteria (2017 revision); 3. Age ≥18 years; 4. No evidence of relapse at least a month preceding the evaluation; 5. No history of medical condition other than MS, which could affect the cognitive ability; 6. Proficiency in Georgian language.

Demographic and clinical data were obtained for each patient from the medical records. All patients were evaluated by one neurologist. After the administration of MoCA, patients completed Beck Depression Inventory (BDI). Finally, physical disability status was measured using the Expanded Disability Status Score (EDSS). All participants completed MoCA. BDI was administered to 44 patients.

Patients who gained 17-22 points on MoCA were considered to have mild to moderate CI, as recommended by the validation study of Georgian language MoCA [8]. Patients obtaining 16 or less points were classified as severely impaired.

Individual scores of each subtest, such as visuospatial abilities, naming, attention, language, abstraction, delayed recall memory and orientation were analyzed. Patients who scored zero on trial making or abstraction subtests were considered to have executive dysfunction. Patients who scored zero on verbal fluency subtests were considered to have impaired verbal fluency. We also identified patients who scored less than 50% of the total score on the visuospatial, naming, attention, language, delayed memory and orientation subtests. Variables are reported as mean±SD and percentage. The internal consistency of the MoCA was measured with the Cronbach's alpha. Correlations between MoCA subtests and the final score of the test were calculated using the Pearson's correlation coefficient (r). Relationships between categorical variables was calculated using Chi square statistics. Multiple linear regression analysis was used to assess the predictors of CI.

Results and discussion. The main characteristics of the study population are outlined in Table 1. The mean age of the subjects was 39.0±9.8 years. Most patients were female (69.8%). Thirty-nine (73.6%) patients had a higher education level. Thirty-nine percent of the subjects were unemployed. Most patients (81.1%) were diagnosed with relapsing-remitting MS (RRMS). The mean disease duration was 6.1±5.1 years, and the mean EDSS score was 3.1±1.5. Among the patients, 56.6% were on disease-modifying treatment (DMT), while the remaining 43.4% had never received it. Clinically significant depression, defined as ≥19 scores on BDI, was identified in nine patients (20.5%).

Table 1. Characteristics of the study population

	MS patients
Number of participants *n*	53
Age (y), mean ± SD	39.0 (±9.8)
Women *n* (%)	37 (69.8%)
Men *n* (%)	16 (30.2)
Education (y), mean ± SD	14.2 ± 1.9
Education ≥15 y, *n* (%)	39 (73.6%)
Education ≤14 y, *n* (%)	14 (26.4%)
Employed *n* (%)	32 (60.4%%)
Unemployed *n* (%)	21 (39.6%)
Disease duration (y), mean ± SD	6.1 ± 5.1
EDSS score, mean ± SD	3.1 ± 1.5
MS subtype	
RRMS *n* (%)	43 (81.1%)
SPMS *n* (%)	8 (15.1%)
PPMS *n* (%)	2 (3.8%)

PPMS - primary progressive multiple sclerosis; RRMS - relapsing remitting multiple sclerosis; SD - standard deviation; SPMS - secondary progressive multiple sclerosis

Table 2. Mean scores of MoCA and its subtests. Correlation of MoCA subtests with the final MoCA score.

	Mean score±SD	***P value***	**Pearson's r**	**P value**
MoCA	**22.9±3.7**	***<0.0001***	**-**	**-**
Visuospatial/Executive	3.8±1.2	*0.1*	0.714	<0.0001
Naming	2.9±0.3	*0.4*	0.154	0.3
Attention	5.1±1.0	*0.2*	0.502	<0.0001
Language	1.8±0.8	*0.2*	0.510	<0.001
Abstraction	0.9±0.7	*0.2*	0.403	0.002
Delayed Memory	2.5±0.7	*0.2*	0.651	<0.0001
Orientation	5.9±0.6	*03*	0.220	0.1

Table 3. Logistic regression analysis for various factors affecting cognitive status in patients with MS

	Coefficient	Odds Ratio	95% CI	*p*
Age	0.0162	1.0164	0.9517 - 1.0854	0.6287
Education (years)	**-0.2943**	**0.7450**	0.5404 - 1.0272	**0.0325**
Duration	0.0022	1.0022	0.8830 - 1.1376	0.9726
EDSS	**0.5015**	**1.6512**	1.0272 - 2.6545	**0.0384**
Progressive course	**0.2077**	**1.2308**	**1.0166 - 1.4901**	**0.0333**

Table 2 shows the mean scores of MoCA and all subtests. In general, twenty-two subjects (41.5%) received abnormal scores on MoCA. Nineteen patients (35.8%) scored 22 to 17, and were therefore classified as having mild to moderate CI. Three patients (5.7%) obtained ≤ 16 points and were regarded as severely impaired.

Number of patients, who received low scores on individual subtests of the MoCA, was 41 (77.4%). Most of the patients (50.9%) failed the delayed memory test, twenty-two (41.5%) patients had zero scores on any of the subtests evaluating executive function (Trial making, Abstraction), 15 subjects (28.3%) received zero score on verbal memory test, nine patients (17%) failed visuospatial subtest and 4 (7.5%) patients showed impaired attention.

The test showed good internal consistency (Cronbach's alpha 0.68). All subtests were positively correlated with the final MoCA score, and two subtests, Visuospatial/Executive and Delayed memory, demonstrated the strongest positive correlation (Pearson's r = 0.714 and 0.651 respectively, p < 0.0001).

We could not identify any correlation between BDI scores and cognitive outcome, however the prevalence of clinically significant depression was higher among subjects with CI compared to those without cognitive decline (22.7% vs. 12.9%).

We used multiple regression analysis to identify predictors of CI in patients with MS. We found a moderate, but statistically significant correlation between education years, EDSS score, progressive disease course, and CI in MS patients (Table 3). A chi-square test of independence showed a significant association between CI and unemployment X^2 (2, N=53) = 4.5, p < .034. The proportion of patients with cognitive decline did not differ by DMT status X^2 (2, N=53) = 0.2, p < .64.

Evidence from current research suggests that CI is very common in patients with MS, affecting 22%-70% of patients with MS [9,14]. It substantially impacts the daily and working abilities of patients and is one of the main predictors of occupational disability [4]. Timely identification of cognitive dysfunction ensures adequate management of MS patients and might improve their quality of life.

Thorough neuropsychological assessment is time-consuming, costly, and requires the presence of neuropsychological service at the site. There is an urgent need for sensitive and reliable screening instruments in MS that would address specific aspects of CI in this population [12].

MoCA is the most widely used screening test for MCI. Validity and reliability of the test have been investigated in many neurological conditions [10]. There are few studies that have addressed the application of MoCA in MS patients and found that it correlates well with standardized neuropsychological instruments, specifically developed for MS [2,6,11]. One of the main advantages of MoCA is that it evaluates two commonly affected cognitive domains, i.e., the executive system and verbal memory.

This was the first study to evaluate the prevalence of CI in Georgian patients with MS using MoCA. The overall prevalence of CI in our MS group was 41.5%. Moreover, 35.8% of subjects had mild to moderate CI, which is three times higher than that reported previously by a population-based study in Georgia [7]. Severe cognitive impairment was identified in 5.7% of the patients. As expected, MS patients most commonly failed the subtests evaluating delayed memory and executive system. Our results are compatible with the recent multi-center study by Ruano et al., revealing CI in 46% of MS patients. Executive function was reported to be the second most commonly affected cognitive sphere in this cohort [15].

Disease modifying drugs reduce activity and progression of MS, but their impact on cognitive status of MS patients is unclear. We could not find any association between DMT and cognitive outcome. In our study, proportion of subjects with CI was similar among treatment naïve patients and those who were under continuous DMT.

We found significant association between CI and unemployment. Number of jobless patients was twice as high in CI group. Clinically significant depression was more common among patients with CI, indicating potential negative impact of depression on cognitive functioning. We found that lower education status, higher physical disability and progressive disease course are the main risk factors for CI in patients with MS.

Conclusion. Prevalence of CI is reasonably high among patients with MS and should warrant implementation of regular cognitive assessment with valid psychometric instruments. Depression is more common in cognitively impaired MS patients and should be addressed appropriately.

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SUMMARY

EVALUATION OF COGNITIVE IMPAIRMENT IN PATIENTS WITH MULTIPLE SCLEROSIS USING GEORGIAN LANGUAGE MONTREAL COGNITIVE ASSESSMENT

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The main objective of the study was to evaluate the prevalence and risk factors of cognitive impairment in patients with multiple sclerosis.

Fifty-three patients with multiple sclerosis were enrolled in this cross-sectional study. Study participants underwent neurological status examination and cognitive screening with Montreal Cognitive Assessment. Beck Depression Inventory was used to assess mental health. Statistical analysis was performed using SPSS software, version 26.0.

The overall prevalence of cognitive impairment in our group was 42%. We found that higher physical disability and progressive disease course are main risk-factors for cognitive decline in patients with multiple sclerosis.

Keywords: cognitive impairment, multiple sclerosis, risk-factors.

РЕЗЮМЕ

ОЦЕНКА КОГНИТИВНЫХ НАРУШЕНИЙ У ПАЦИЕНТОВ С РАССЕЯННЫМ СКЛЕРОЗОМ ПРИ ПОМОЩИ МОНРЕАЛЬСКОЙ ШКАЛЫ ОЦЕНКИ КОГНИТИВНЫХ ФУНКЦИЙ

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Целью исследования явилось изучение распространения когнитивных нарушений у пациентов с рассеянным склерозом. В кросс-секционное исследование включено 53 па-

циента с рассеянным склерозом. Пациентам проведен неврологический осмотр и когнитивная оценка при помощи Монреальской шкалы оценки когнитивных функций. С целью скрининга депрессии они заполнили опросник депрессии Бека. Статистический анализ исследования проведен при помощи программы SPSS v26.

Распространение когнитивных нарушений в группе исследования составило 42%. Результаты проведенного исследования выявили, что высокая степень ограничения физической способности и прогрессивная форма заболевания являются главным риск-фактором когнитивных нарушений у пациентов с рассеянным склерозом.

რეზიუმე

კოგნიტური დისფუნქციის კვლევა პაციენტებში გაფანტული სკლეროზით მონრეალის შეფასების სკალის გამოყენებით

[1]ნ. ბოჭორიშვილი, [2]ნ. მიქელაძე, [1]ა. ძაგნიძე, [2]ნ. მიქავა, [1]მ. ჯანელიძე

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[2]ს. ხეჩინაშვილის სახ. საუნივერსიტეტო კლინიკა, თბილისი, საქართველო

კვლევის მიზანს წარმოადგენდა პაციენტებში გაფანტული სკლეროზით კოგნიტური დაზიანების გავრცელების და მისი რისკ-ფაქტორების შესწავლა.

წინამდებარე ჯვარედინ-სექციურ კვლევაში ჩართული იყო 53 პაციენტი გაფანტული სკლეროზით. საკვლევ პირებს ჩაუტარდა ნევროლოგიური გასინჯვა და კოგნიტური დაზიანების სკრინინგი მონრეალის კოგნიტური შეფასების სკალის მეშვეობით. ფსიქიკური სტატუსის შეფასების მიზნით მათ შეავსეს ბეკის კითხვარი.

კვლევის სტატისტიკური ანალიზი ჩატარდა SPSS v26 პროგრამის მეშვეობით.

კოგნიტური დისფუნქციის გავრცელებამ კვლევის ჯგუფში შეადგინა 42%, რაც შეესაბამება ლიტერატურაში აღწერილ მონაცემებს. გამოვლინდა, რომ პაციენტებში გაფანტული სკლეროზით ფიზიკური უნარშეზღუდულობის მაღალი ხარისხი და დაავადების პროგრესული ფორმა წარმოადგენს კოგნიტური დაზიანების მთავარ რისკ-ფაქტორს.

КЛИНИКО-МАТЕМАТИЧЕСКИЙ АНАЛИЗ ВЗАИМООТНОШЕНИЙ МЕЖДУ ХАРАКТЕРОМ ПРОГНОЗА И ОСОБЕННОСТЯМИ ДЕБЮТОВ ПРИ РАЗНЫХ ТИПАХ ТЕЧЕНИЯ РАССЕЯННОГО СКЛЕРОЗА

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Вопрос о диагностическом значении клинических показателей дебюта при рассеянном склерозе (РС) и его роль в дальнейшем формировании особенностей течения и прогноза этого заболевания является недостаточно изученным и дискуссионным [8-10,13,16,17,20]. Прогноз, как ожидаемый результат предшествующего течения заболевания, носит интегративный характер и зависит от клинической интерпретации всей картины болезни в целом, включая ретроспективный анализ этапов заболевания во временном аспекте, т.е., по существу, представляет собой экспертную оценку, проведенную врачом-неврологом [5-7,13,15,18].

Известно, что характер прогноза при рецидивирующем течении (РТ), в целом, расценивается как благоприятный. Однако при этом типе течения существуют многообразные варианты, отличающиеся своим клиническим звучанием и прогностической значимостью. Так, наличие клинических маркеров, свидетельствующих о риске высокой трансформации во вторично-прогредиентное течение (ВПТ), позволяет трактовать текущий прогноз при РТ как неопределенный.

У больных с прогредиентными типами течения (ПТТ), которые, в основном, характеризуются быстрыми темпами накопления неврологического дефицита и высокой степенью инвалидизации, в подавляющем большинстве случаев формируется неблагоприятный прогноз [4,5]. Однако даже при этих типах течения у части больных следует выделять относительно «доброкачественный» вариант прогноза – неопределенный, имеющий характерные особенности, ведущими из которых является длительный период рецидивирующего этапа при ВПТ, медленное поступательное накопление неврологического дефицита на этапе вторичного и первичного прогрессирования, положительный ответ на различные методы патогенетической и симптоматической терапии.