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CHRONIC ALCOHOL-INDUCED ENCEPHALOPATHY: PREDICTORS OF COGNITIVE IMPAIRMENT AND FUNCTIONAL DISABILITY

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Summary

Introduction: Predicting the risk of cognitive dysfunction and disability in everyday life among chronic alcohol-induced encephalopathy (CAIE) patients allows timely treatment to prevent dementia.
The aim: to develop a mathematical model for predicting the risk of developing cognitive disorders and functional disability in patients with CAIE based on the analysis of polymorphic variants of the genes *ACE*, *AT2R1*, *eNOS*, *PON1*, *IL-1*β, *IL-10*, *TNF-*α, as well as cofactors (gender, age group, the disease duration, and presence/absence of somatic comorbidity).
Materials and methods: We examined the 102 patients with CAIE who were undergoing inpatient treatment in the communal non-profit enterprise «Ternopil Regional Clinical Psychoneurological Hospital» during 2021-2022 and were included in the retrospective analysis. The molecular-genetic testing was performed for 26 patients of the general group. The molecular-genetic differentiation of the studied polymorphic variants of genes was carried out in the molecular-genetic laboratory of the state institution «Reference Centre for Molecular Diagnostics of the Ministry of Health of Ukraine», Kyiv. Cognitive functions were assessed using the Montreal Cognitive Test (MoCA); activities of daily living were assessed using the Barthel index. A logistic regression analysis was performed to determine the risk of cognitive impairment and functional disability developing in patients with CAIE.
Results: Analyzing polymorphic variants of the *ACE, AT2R1, eNOS, PON1, IL-1*β, *IL-10, TNF-*α genes, as well as such cofactors as gender, age group, history and presence/absence of somatic comorbidity in the context of the development of cognitive disorders in patients with CAIE it has been established that the C108T polymorphism of the *PON1* gene has the most significant prognostic value (in the presence of the T/T genotype, the probability of cognitive impairment is 39.84 %). At the same time, carriage of both the T allele and the C allele of the *PON1* gene is associated with a significant decrease in the MoCA score. Regarding the development of functional disability in patients with CAIE, the C108T polymorphism of the *PON1* gene also has the most significant prognostic value (in the presence of the T/T genotype, the probability of functional disability is 48.08 %, respectively, C/C – 30.96 % and CT – 39.22 %, however, no statistically significant differences in the Barthel index values were found in carriers of the above genotypes).
Conclusions: It was established that the C108T polymorphism of the *PON1* gene is significantly associated with the development of cognitive impairment and functional disability in patients with CAIE, which indicates the feasibility of further studies involving a larger sample of patients.

Key words: **chronic alcohol-induced encephalopathy, cognitive dysfunction, functional disability, gene polymorphism, prognosis**

INTRODUCTION

Long-term consumption of alcohol can lead to the development of various diseases and exacerbate their symptoms. Studies show that individuals who consume alcohol for extended periods of time have a higher relative risk of mortality from all causes compared to the general population [1, 2]. Specifically, in 2016, alcohol use

was associated with 3 million deaths and 132.6 million disability-adjusted life years [3]. In addition, alcohol is one of the most important causes of premature mortality; alcohol consumption caused 14.6 % of all premature deaths of adults in eight European countries, 17.3 % among men and 8.0 % among women [4].

According to the World Health Organization (WHO), 2.3 billion people in the world currently consume alcohol excessively. Between 2005 and 2016, the global per capita alcohol consumption increased from 5.5 to 6.4 liters, and it is expected to reach 7.6 liters by 2030 [3, 5, 6]. In addition, studies conducted across Europe between April to June 2020 showed an increase in per capita alcohol consumption, likely due to social isolation during the SARS-CoV-2 pandemic [7]. In 2016, the average annual alcohol consumption in Ukraine was 8.6 liters per person. About 4.2 % of adult Ukrainians have alcohol-related problems, which is significantly higher than in most developed European countries [8, 9]. T. M. Roschupkina reports that one out of every five Ukrainians consumes alcohol in excess of the permitted limit, which is 2 liters of pure alcohol annually. The most common age group that indulges in excessive drinking is young adults between the ages of 18 and 29 [10].

Chronic alcohol abuse can lead to various neurological disorders, including chronic alcoholic encephalopathy (CAIE). According to several studies [11-13], CAIE is characterized by cognitive disorders, progressive impairment of intellectual functions, and in over 10.0 % of patients, it can lead to dementia. It is noteworthy that in a recent meta-analysis (2019), J. Rehm et al. showed that there are possible links not only between chronic alcohol abuse (defined as the consumption of more than 60 g of pure alcohol per day for men and more than 40 g of pure alcohol per day for women) but also between irregular alcohol consumption and an increased risk of cognitive impairment or dementia [14]. Patients diagnosed with dementia require round-the-clock physical and psychological care, which leads to significant economic losses [15]. Therefore, predicting an individual's risk of developing cognitive dysfunction and functional failure due to CAIE can allow for timely treatment to prevent the development of dementia. In order to accurately assess the risk of encephalopathy and its progression, it is vital to have a thorough understanding of the disease's genetic basis. Allelic polymorphism refers to the variations in an individual's genome that determine their unique characteristics. These variations are caused by point changes in genes or tandem repeats in varying quantities. They can either determine resistance to certain diseases or predispose an individual to certain pathologies, including encephalopathy [16].

THE AIM OF THE STUDY

To develop a mathematical model that can predict the risk of cognitive impairment and functional disability developing in patients with CAIE. The model was based on the analysis of polymorphic variants of genes such as *ACE*, *AT2R1*, *eNOS*, *PON1*, *IL-1*β, *IL-10*, *TNF*-α, as well as cofactors including gender, age category, catamnesis, and the presence/absence of somatic comorbidity.

MATERIALS AND METHODS

During the years 2021-2022, a total of 102 patients with CAIE who received inpatient treatment under the communal non-profit enterprise «Ternopil Regional Clinical Psychoneurological Hospital» were examined and included in the retrospective analysis. Out of these 102 patients, 26 underwent molecular genetic testing. The control group consisted of 12 healthy individuals who were representative in terms of age and sex. Given the lack of a universal classification system for encephalopathies and their respective severities, which accounts for the origin and clinical presentation of each type, the confirmation of CAIE was established using the criteria proposed by multiple researchers [17, 18].

Inclusion criteria of patients: age from 18 to 75 years; patients who systematically abuse alcohol for more than 5 years, with alcohol addiction; establishing the relationship between alcohol consumption and clinical and neurological symptoms; availability of the patient's informed consent.

Exclusion criteria of patients: absence of alcohol addiction; the presence of oncological pathology; the presence of concomitant somatic pathology in the stage of decompensation; use of psychoactive substances; experienced traumatic brain and skull damage of varying degrees of severity; the presence of other diseases that could be the cause of psychoneurological disorders, behavioral and mental disorders; present encephalopathy of any other genesis.

The research was approved by the Commission of Bioethical Expertise and Research Ethics of the I. Horbachevsky Ternopil National Medical University, Ministry of Health, Ukraine. (report № 74 dated September 1st, 2023).

The polymorphic variants of genes were analyzed for molecular and genetic differentiation using allele-specific PCR or PDRF PCR (restriction fragment length polymorphism) methods. These methods follow standard operating protocols developed by the molecular genetic laboratory of the state institution «Reference Center for Molecular Diagnostics of the Ministry of Health of Ukraine» in Kyiv. The protocols are based on scientific publications available in open sources [19-22], table 1.

The Montreal Cognitive Assessment (MOCA) was used to evaluate the cognitive functions of all participants. The assessment followed the standard procedure for evaluating cognitive domains, with a maximum possible score of 30. A score of 26 or higher is considered normal, while a score of 22-25 indicates mild cognitive impairment, 19-21 points indicate moderate impairment, and scores lower than 19 indicate dementia [23].

Table 1

Molecular and genetic differentiation of studied gene variants

№	Gene	International name genetic polymorphism, rs	Link to the source
1.	*IL-1*ß	C3953T, g.8967C>T, rs1143634	[19]
2.	IL-10	C-592A, g.4433A>C, rs1800872	[20]
3.	*TNF*α	G308A, c.-488G>A, rs180062	[21]
4.	ACE	I/D, c.2306-117_2306-116insAF118569.1: g.14094_14382, rs4340	[21]
5.	eNOS	4a/4b, g.150997188 AGGGGTGAGGAAGT CTAGACCTGCTGC[1], rs61722009	[22]
6.	PON1	C108T, g.5124C>T, rs705379	[19]
7.	AT2R1	A1166C, g.148742201A>C, rs5186	[21]

The Barthel Activities of Daily Living (ADL) Index is used to assess daily life activities. It consists of 10 tasks that are part of daily activities, each with a corresponding point value. A score of «0» indicates the impossibility of completing the task or complete dependence on outside help, «5» means assistance is required, while «10» indicates complete independence from the help of others. Based on the evaluation rules, a total score of 0-20 indicates complete dependence, 21-60 indicates severe dependence, 61-90 indicates moderate dependence, 91-99 indicates light dependence, and 100 points indicates complete independence in everyday life activities [23].

For statistical data analysis, we used Microsoft Excel and STATISTICA 13.0 computer software. To accomplish our goal, we conducted a logistic regression analysis with a dependent binary variable. The variable measured the presence (Y=1) or absence (Y=0) of cognitive impairment or functional disability in patients suffering from CAIE. The basic model (Model 1) included polymorphic variants of the studied genes – *ACE, AT2R1, eNOS, PON1, IL-1*β*, IL-10, TNF*-α, which became independent variables. Model 2 included allelic variants of the *ACE, AT2R1, eNOS, PON1, IL-1*β*, IL-10, and TNF*-α genes. Only prognostically important genotypes were included in model 3, as well as the following cofactors (covariants) – the patient's gender (male, female), his age category (young age – 18-44 years; average age – 45-59 years; old age – 60-74 years old; senile age – 75 years and older); catamnesis (up to 1 year; 1-5 years; 6-10 years; more than 10 years), as well as the presence or absence of concomitant somatic diseases.

A logistic regression equation was created to estimate the probability of cognitive impairment and functional disability in patients with CAIE:

The risk of developing cognitive disorders = 1/(1+ex);

The risk of developing functional incapacity = 1/(1+ex),

where e is a mathematical constant of 2.72;

x – a combination of statistically probable predictors;

x=a + b1*Y1 + b2*Y2 + bn*Yn;

a – constant of the model;

b1, b2, bn – coefficients calculated during regression analysis;

Y1, Y2, Yn are categorical values of statistically probable predictors.

Predictors with $p<0.05$ in the regression model were considered statistically significant. Risk for cognitive impairment and functional disability was calculated as a percentage (%).

RESULTS AND DISCUSSION

Based on the logistic regression analysis, the *PON1* gene's C108T polymorphism is associated with cognitive disorders in CAIE patients (Table 2).

With CAIE for model 1, the formula for calculating the value of X will have the following form:

X=1.31+(–0.30)*X1;

where categorical variables:

X1 – 1 – the presence of the SS genotype of the *PON1* gene; 2 – the presence of the CT genotype of the *PON1* gene; 3 – the presence of the TT genotype of the *PON1* gene.

Therefore, in the presence of the TT genotype of the *PON1* gene, the probability of cognitive impairment in patients with CAIE will be 39.84 %. At the same time, in the presence of the CC genotype of the *PON1* gene, this risk will be 26.67 %, and in the presence of the CT heterozygous *PON1* gene, this risk will be 33.00 %.

With CAIE for model 2, the formula for calculating the value of X will have the following form:

X=(1.22)+(–0.32)*X1;

where categorical variables:

X1 – 1 – presence of allele C of the *PON1* gene; 2 – the presence of the T allele of the *PON1* gene.

Therefore, with the presence of the *PON1* gene T risk allele, patients with CAIE have a 35.84 % probability of experiencing cognitive impairment.

Table 2

Results of logistic regression analysis regarding the development of cognitive impairment in patients with CAIE

Factor	Model 1				Model 2			
	Genotype				Allele			
	β	SE	t	p	β	SE	t	p
Constant	1.31	0.39	3.37	0.003*	1.22	0.29	4.18	<0.001*
ACE	-0.08	0.16	-0.52	0.606	0.08	0.14	0.61	0.546
AT2R1	0.25	0.16	1,57	0.134	0.16	0.14	1.17	0.248
eNOS	-0.07	0.09	-0.84	0.412	-0.08	0.11	-0.76	0.449
*IL1*β	0.06	0.25	0.24	0.813	-0.19	0.21	-0.87	0.388
*TNF*α	0.28	0.23	1.23	0.233	0.31	0.21	1.48	0.146
IL10	-0.02	0.13	-0.17	0.865	0.07	0.15	0.48	0.631
PON1	-0.30	0.11	-2.80	0.012*	-0.32	0.11	-2.96	0.005*

Note 1: β – logistic regression coefficient, SE – standard error; t is the value of the Wald test; p – probability coefficient.
Note 2. * is a statistically significant result

Our study results indicate that the *PON1* gene polymorphism remains significant in the occurrence of cognitive disorders in CAIE, even when considering covariates (Table 3).

Table 3

Results of logistic regression analysis regarding the development of cognitive disorders in patients with CAIE, taking into account gender, age category, presence of somatic comorbidity, and catamnesis

Factor	Model 3			
	β	SE	t	p
Constant	2.33	0.50	4.62	<0.001*
PON1	-0.40	0.13	-3.21	0.004*
Sex	-0.28	0.21	-1.37	0.186
Age category	-0.06	0.10	-0.64	0.533
Somatic comorbidity	0.18	0.14	1.24	0.228
Disease duration	0.03	0.06	0.45	0.660

Note 1: β – logistic regression coefficient, SE – standard error; t is the value of the Wald test; p – probability coefficient. Note 2. * is a statistically probable result

Patients who carry both risk alleles of the *PON1* gene exhibit a significant decrease in scores on the Montreal cognitive test, compared to individuals who do not carry these risk alleles (Table 4).

Table 4

The results of the analysis of cognitive functions in patients with CAIE based on the Montreal cognitive test MOCA depending on the carrier of risk alleles of the PON1 gene

Group	Range of fluctuations of indicators, points		Total points	p
	Min	Max		
Absence of risk alleles of the *PON1* gene	25	26	25.67±0.58	p_{1-3} <0.05* $p_{1-2, 2-3}$ >0.05
Carrier of one risk allele of the *PON1* gene	10	26	21.50±4.35	
Carrier of 2 risk alleles of the *PON1* gene	2	23	17.78±4.35	

Note: * is a statistically significant result

It should be emphasized that the development of functional disability in CAIE patients is also due to *PON1* gene polymorphism (tables 5, 6). Based on the presence of the TT genotype of the *PON1* gene, it is expected that 48.08 % of patients with CAIE will experience functional disability. On the other hand, patients with the CC genotype of the *PON1* gene are likely to suffer from functional disability in 30.96 % of cases, while those with the heterozygous *PON1* gene will experience it in 39.22 % of cases. However, after a multifactor analysis of the impact of the alleles of the studied genes, no reliable predictor of the development of functional disability associated with CAIE was established (Table 9.16).

Analysis of Barthel index results did not show significant differences among patient groups with different PON1 gene polymorphisms ($p > 0.05$), (Table 7).

Table 5

Results of logistic regression analysis regarding the development of functional disability in daily life in patients with CAIE

Factor	Model 1				Model 2			
	Genotype				Allele			
	β	SE	t	p	β	SE	t	p
Constant	1.16	0.59	1.97	0.044*	0.55	0.42	1.29	0.204
ACE	-0.27	0.24	-1.11	0.280	0.01	0.20	0.06	0.952
AT2R1	-0.12	0.24	-0.50	0.624	-0.04	0.20	-0.21	0.831
eNOS	-0.20	0.14	-1.49	0.153	-0.19	0.15	-1.23	0.224
*IL1*β	0.35	0.38	0.93	0.367	-0.08	0.31	-0.26	0.797
*TNF*α	0.35	0.35	0.99	0.335	0.42	0.31	1.37	0.178
IL10	0.15	0.20	0.75	0.461	0.23	0.22	1.04	0.303
PON1	-0.36	0.16	-2.20	0.041*				

Note 1: β – logistic regression coefficient, SE – standard error; t is the value of the Wald test; p – probability coefficient.
Note 2. * is a statistically significant result

Table 6

The results of logistic regression analysis regarding the development of functional disability in everyday life in patients taking into account gender, age category, presence of somatic comorbidity, as well as catamnesis

Factor	Model 3			
	β	SE	t	p
Constant	2.27	0.68	3.34	0.003*
PON1	-0.56	0.17	-3.30	0.004*
Sex	-0.51	0.28	-1.84	0.081
Age category	-0.14	0.13	-1.07	0.298
Somatic comorbidity	0.28	0.19	1.45	0.163
Disease duration	0.04	0.08	0.49	0.631

Note 1: β – logistic regression coefficient, SE – standard error; t is the value of the Wald test; p – probability coefficient.
Note 2. * is a statistically significant result

Table 7

The results of the analysis of functional disability in everyday life based on the analysis of the Barthel index in patients with CAIE depending on the carrier of risk alleles of the PON1 gene

Group	Range of fluctuations of indicators, points		Total points	p
	Min	Max		
Absence of risk alleles of the PON1 gene	100	100	100.00±0.00	$p_{1-2, 1-3, 2-3} > 0.05$
Carrier of one risk allele of the PON1 gene	90	100	96.07±4.01	
Carrier of 2 risk alleles of the PON1 gene	90	100	94.44±3.91	

Alcohol abuse is a necessary factor in the development of brain diseases due to the diverse mechanisms of ethanol neurotoxicity [24]. There are two main ways in which alcohol abuse can harm the brain. First, both ethanol and acetaldehyde, which is a byproduct of ethanol metabolism, have a direct toxic effect on the brain. This can lead to permanent damage to the brain's structure and function [25]. Second, long-term alcohol abuse can cause a deficiency in thiamine, which is an essential nutrient for the brain. This deficiency can result from inadequate dietary intake, poor absorption in the intestinal tract, and impaired use by the cells. This can lead to Wernicke-Korsakoff syndrome, a condition that affects memory, vision, and muscle coordination [26].

Treatment with thiamine can reverse many symptoms of Wernicke-Korsakoff syndrome. However, certain chronic neuropsychological consequences of previous thiamine deficiency may persist even with appropriate treatment [27]. Alcohol abuse poses a significant risk to the brain by contributing to other pathologies such as hepatic encephalopathy in patients with liver cirrhosis, epilepsy, or head trauma. Additionally, alcohol abuse indirectly increases the risk of vascular dementia by its association with cardiovascular risk factors and diseases such as high blood pressure, coronary heart disease, cardiomyopathy, atrial fibrillation, and stroke [28]. These associations have been identified as causal and have been confirmed by studies conducted on individuals with alcohol use disorders [29].

Alcohol abuse is associated with a higher likelihood of developing risk factors for dementia, such as lower levels of education, tobacco smoking, and depression [14].

It's important to note that CAIE is usually accompanied by severe somatoneurological problems, and its treatment is generally ineffective. Therefore, studying the genetic basis of the disease and predicting its course is crucial in order to offer timely and appropriate treatment to prevent dementia. For this reason, our research has focused on identifying genes that may be linked to the development of cognitive impairment and functional disability in CAIE.

After conducting a logistic regression analysis of various genes and factors that may affect cognitive disorders, it was found that the PON1 gene polymorphism has the greatest prognostic value. Specifically, in the presence of the T/T genotype, the probability of cognitive disorders is 39.84 %. Other factors that were analyzed include ACE, AT2R1, eNOS, IL-1β, IL-10, TNF-α genes, as well as gender, age category, catamnesis, and the presence/absence of somatic comorbidity. At the same time, individuals who carry both the T allele and the C allele of the PON1 gene are likely to have a lower score on the MOCA scale. Additionally, the C108T polymorphism of the PON1 gene has the highest predictive value in the development of functional disability in patients with CAIE. Those with a T/T genotype have a 48.08 % probability of functional disability, while those with a C/C genotype have a 30.96 % probability and those with a C/T genotype have a 39.22 % probability. However, no statistically significant differences were found in the Barthel index among carriers of these genotypes. Regarding sex, age category, catamnesis, and the presence/absence of somatic comorbidity, these covariates do not affect the prognostic significance of the C108T polymorphism of the PON1 gene in the context of the development of both cognitive dysfunction and functional disability in patients with CAIE.

Paraoxonase 1 (PON1) is an enzyme that is dependent on calcium and hydrolytic in nature. It is expressed in various organs of the human body, including the brain, kidney, liver, and colon. It circulates in the blood and is bound to the high-density lipoprotein subfraction [30]. In our previous study, we analyzed the distribution of allele frequencies of the –108C/T polymorphic variant of the *PON1* gene in patients with CAIE compared to healthy individuals [31]. We found probable discrepancies in the frequency of allele C (38.46 % vs. 66.67 %) and allele T (61.54 % versus 33.33 %) (p=0.028) between the two groups. Analyzing the odds ratio and its confidence interval (95 % CI) for the –108C/T polymorphic variant of the PON1 gene in patients with CAIE, it was found that the presence of the T allele increases the risk of encephalopathy development and/or progression by 3.2 times (95 % CI 1.16-8.84).

M. E. Bednarska-Makaruk et al. have demonstrated that the activity of PON1 is significantly lower in dementia patients, especially in neurodegenerative dementia (such as Alzheimer's disease and mixed dementia), as compared to the controls [32]. The study found that the number of carriers of the PON1-108T allele was significantly higher in the Alzheimer's group than in the control group. The researchers also discovered that the activity of the PON1 enzyme was highest in carriers of the C/C genotype and lowest in carriers of the T/T genotype. This suggests that the 108C/T polymorphism of the PON1 gene plays a significant role in the risk of developing dementia, with low PON1 activity having a dominant effect on this risk. Another study by M. Saeidi et al. demonstrated that the C-108T promoter region of the PON1 gene is associated with the development of Alzheimer's disease. Patients with Alzheimer's disease were found to have a higher frequency of the T allele, and the homozygous genotype (T/T) was associated with low PON1 arylesterase activity [33].

CONCLUSIONS

An analysis was conducted on polymorphic variants of genes such as *ACE, AT2R1, eNOS, PON1, IL-1β, IL-10, and TNF-α*, as well as cofactors such as gender, age category, and history and presence/absence of somatic comorbidity. This was done in order to determine their role in the development of cognitive disorders in patients with CAIE. The study concluded that the *PON1* gene's C108T polymorphism has the highest prognostic value, with a 39.84 % probability of cognitive impairment in individuals with the T/T genotype. Additionally, carriers of both the T allele and the C allele of the *PON1* gene are likely to have a decrease in the number of points on the MoCA scale. In patients with CAIE, the development of functional disability is significantly impacted by the *PON1* gene's C108T polymorphism. Those with the T/T genotype have a higher probability (48.08 %) of developing functional disability than those with the C/C genotype (30.96 %) or the C/T genotype (39.22 %). However, despite these differences, there was no significant correlation found between the above-mentioned genotypes and the Barthel index. Based on these findings, it is likely that the C108T polymorphism of the *PON1* gene is associated with both cognitive impairment and functional disability in patients with CAIE.

Prospects for further research. To validate these findings, it is essential to conduct further research using a larger patient sample. Additionally, in the future, it would be advisable to analyze prognostic markers for other types of encephalopathies to compare the results obtained in this study. This will help optimize the treatment tactics for encephalopathies.

COMPLIANCE WITH ETHICAL REQUIREMENTS

The study was conducted in accordance with the principles of the Helsinki Declaration of the World

Medical Association «Ethical principles of medical research involving a person as an object of research». All study participants provided informed consent in writing to participate in the study.

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The author declares that there is no conflict of interest. Source of funding – self-funded.

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Резюме

ХРОНІЧНА АЛКОГОЛЬ-ІНДУКОВАНА ЕНЦЕФАЛОПАТІЯ: ПРЕДИКТОРИ РОЗВИТКУ КОГНІТИВНИХ ПОРУШЕНЬ ТА ФУНКЦІОНАЛЬНОЇ НЕСПРОМОЖНОСТІ

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Вступ. Прогнозування індивідуального ризику розвитку когнітивної дисфункції та функціональної неспроможності у повсякденному житті у пацієнтів з хронічною алкоголь-індукованою енцефалопатією (ХАЕ) дозволить своєчасно призначити адекватне лікування для запобігання розвитку деменції.
Мета: розробити математичну модель прогнозування ризику розвитку когнітивних порушень та функціональної неспроможності у пацієнтів з ХАЕ на основі аналізу поліморфних варіантів генів *ACE, AT2R1, eNOS, PON1, IL-1β, IL-10, TNF-α,* а також кофакторів (стать, вікова категорія, катамнез та наявність/відсутність соматичної коморбідності).
Матеріали та методи. Обстежено 102 пацієнти з ХАЕ, які перебували на стаціонарному лікуванні на базі комунального некомерційного підприємства «Тернопільська обласна клінічна психоневрологічна лікарня» впродовж 2021-2022 рр. та яких включили у ретроспективний аналіз, з них 26 хворим проводили молекулярно-генетичне дослідження. Молекулярно-генетичну диференціацію досліджуваних поліморфних варіантів генів здійснювали в молекулярно-генетичній лабораторії державного закладу «Референс-центр з молекулярної діагностики МОЗ України», м. Київ. Когнітивні функції оцінювали за допомогою Монреальського когнітивного тесту (МоСА); повсякденну життєдіяльність оцінювали за допомогою індекса Бартела. Для оцінки ризику розвитку виникнення когнітивних порушень та функціональної неспроможності у пацієнтів із ХАЕ проведено логістичний регресійний аналіз.
Результати. Аналізуючи поліморфні варіанти генів *ACE, AT2R1, eNOS, PON1, IL-1β, IL-10, TNF-α,* а також кофактори (стать, вікову категорію, катамнез та наявність/відсутність соматичної коморбідності) в контексті розвитку когнітивних порушень у пацієнтів з ХАЕ встановлено, що найбільшу прогностичну цінність має *C108T* поліморфізм гена *PON1* (за наявності генотипу Т/Т ймовірність виникнення когнітивних порушень складає 39,84 %). При цьому носійство як алелі Т, так і алелі С гена *PON1* асоціюється із вірогідним зниженням кількості балів за шкалою МоС А. Щодо розвитку функціональної неспроможності у пацієнтів із ХАЕ, то найбільшу прогностичну цінність також має *C108T* поліморфізм гена *PON1* (за наявності генотипу Т/Т ймовірність виникнення функціональної неспроможності становить 48,08 %, відповідно, С/С – 30,96 % та С/Т – 39,22 %, проте статично значимих відмінностей за індексом Бартела у носіїв вище-вказаних генотипів не виявлено).
Висновки. Встановлено, що *C108T* поліморфізм гена *PON1* вірогідно асоціюються із розвитком як когнітивних порушень, так і функціональної неспроможності у пацієнтів з ХАЕ, що свідчить про доцільність подальших досліджень із залученням більшої вибірки пацієнтів.

Ключові слова: **хронічна алкоголь-індукована енцефалопатія, когнітивна дисфункція, функціональна неспроможність, поліморфізм генів, прогнозування**