# MINISTRY OF EDUCATION AND SCIENCE OF UKRAINE SUMY STATE UNIVERSITY ACADEMIC AND RESEARCH MEDICAL INSTITUTE

### Eastern Ukrainian Medical Journal

116, Kharkivska st., Sumy 40007, Ukraine e-mail: eumj@med.sumdu.edu.ua

eumj.med.sumdu.edu.ua

ISSN: 2663-5909 (print)/2664-4231 (online)

© 2024 by the author(s).

This work is licensed under Creative Commons Attribution 4.0 International License https://creativecommons.org/licenses/by/4.0/



**How to cite / Як цитувати статтю:** Chemych M, Sosnovenko D. Neurotropic properties of retroviruses in the context of anxiety-depressive and cognitive disorders in HIV-positive patients. *East Ukr Med J.* 2024;12(3):651-659

DOI: https://doi.org/10.21272/eumj.2024;12(3):651-659

#### **ABSTRACT**

#### Mykola Chemych

https://orcid.org/0000-0002-7085-5448
Department of Infectious Diseases and Epidemiology, Sumy State University, Sumy, Ukraine

#### Dmytro Sosnovenko

https://orcid.org/0000-0001-6632-0603

Department of Infectious Diseases and Epidemiology, Sumy State University, Sumy, Ukraine

### NEUROTROPIC PROPERTIES OF RETROVIRUSES IN THE CONTEXT OF ANXIETY-DEPRESSIVE AND COGNITIVE DISORDERS IN HIV-POSITIVE PATIENTS

**The aim**: a comprehensive assessment and comparison of the prevalence of undiagnosed anxiety-depressive and cognitive symptoms in HIV-positive individuals at different stages of the disease who have been undergoing treatment for an extended period.

Materials and methods According to the criteria of the scientific project, 71 HIV-positive individuals undergoing outpatient treatment with a compensated condition were involved. To explore dependencies on clinical stages (ClSt) of HIV infection and search for gender differences, the study was divided into 2 stages, respectively. The research included the collection of epidemiological and clinical-anamnestic data, as well as laboratory studies. Clinical-psychopathological and psychometric methods were used. Inclusion criteria for the study were HIV-positive status, receiving ART for more than 6 months, adulthood, and voluntary consent to participate. The obtained information was statistically processed by mathematical methods of statistics, using ANOVA criteria, Student's t-test, etc. Elements of neurocognitive and anxiety-depressive symptomatology were considered, utilizing GAD-7, HADS, and MMSE scales.

**Results:** In patients of different groups in the first stage of the study, a gradually increasing level of anxiety and cognitive impairments was identified, depending on the stage of HIV infection. In the second stage of the study, gender and stage-related differences in anxiety and cognitive disorders were found in patients of all groups.

Conclusions. Individuals in the first clinical stage (I ClSt) exhibited the least anxiety-depressive and cognitive disorders, indicating emotional and cognitive stability at this stage of HIV infection. HIV-infected individuals in the second and third clinical stages (II and III ClSt) demonstrated a progressive tendency toward anxious and depressive disorders, indicating a stage-dependent relationship to the

progression of the disease. Patients in the fourth clinical stage (IV ClSt) showed the most pronounced anxious, depressive, and cognitive symptoms, which may be associated with the duration of the illness and antiretroviral therapy (ART). Research results in the female group (Group A1) suggest their lower susceptibility to disorders compared to males (Group A2) in the early stages of HIV infection. In the later stages (III-IV), it was found that women had pronounced anxious and depressive disorders (Group B1), while men exhibited signs of cognitive and depressive disorders (Group B2).

**Keywords:** neuroAIDS; diagnosis, health, society, tests.

Corresponding author: Dmytro Sosnovenko, Department of Infectious Diseases and Epidemiology, Sumy State University, Sumy, Ukraine; e-mail: <u>d.sosnovenko@kinf.sumdu.edu.ua</u>

#### **РЕЗЮМЕ**

#### Микола Чемич

https://orcid.org/0000-0002-7085-5448 Кафедра інфекційних хвороб з епідеміологією, Сумський державний університет, Суми, Україна

#### Дмитро Сосновенко

https://orcid.org/0000-0001-6632-0603 Кафедра інфекційних хвороб з епідеміологією, Сумський державний університет, Суми, Україна

## НЕЙРОТРОПНІ ВЛАСТИВОСТІ РЕТРОВІРУСІВ У КОНТЕКСТІ ТРИВОЖНО-ДЕПРЕСИВНИХ ТА КОГНІТИВНИХ РОЗЛАДІВ ВІЛ-ПОЗИТИВНИХ ПАЦІЄНТІВ

**Мета:** комплексна оцінка та порівняння поширеності не діагностованої тривожно-депресивної та когнітивної симптоматики у ВІЛ-позитивних осіб на різних стадіях хвороби які перебувають тривалий час на лікуванні.

Матеріали і методи: за критеріями наукового проєкту було залучено ВІЛ-позитивну особу, яка перебувала амбулаторному лікуванні та мала компенсований стан. Для з'ясування залежностей від клінічних стадій (КлСт) ВІЛ-інфекції та пошуку відмінностей за гендерною ознакою роботу було розподілено на 2 етапи, відповідно. Дослідження включало збір епідеміологічних та клініко-анамнестичних даних, досліджень. Було лабораторних використано клінікопсихопатологічний та психометричний методи. Критеріями добору до дослідження слугували ВІЛ-позитивний статус, отримання АРТ понад 6 місяців, повноліття та добровільна згода на участь. Отримана інформація статистично опрацьована математичними методами статистики з використанням критеріїв ANOVA, tкритерію Враховувалися Стьюдента тощо. елементи нейрокогнітивної та тривожно-депресивної симптоматики, використовуючи шкали GAD-7, HADS та MMSE.

**Результати:** у пацієнтів різних груп першого етапу дослідження встановлено поступово зростаючий рівень тривоги та когнітивні порушення, залежно від стадії ВІЛ-інфекції. На другому етапі дослідження виявлено статеві та стадійні відмінності у показниках тривоги та когнітивних розладах у пацієнтів всіх груп.

Висновки. В осіб І КлСт виявляли найменші тривожнодепресивні та когнітивні розлади, що свідчили про емоційну та когнітивну стабільність на цьому етапі ВІЛ-інфекції. ВІЛінфіковані у ІІ та ІІІ КлСт демонстрували прогресуючу тенденцію до тривожних та депресивних розладів, що вказує на залежність від стадії захворювання. Хворі, що мали ІV КлСт виказували найбільш виражені тривожні, депресивні та когнітивні симптоми, що може бути пов'язано з тривалістю хвороби та АРТ. Результати досліджень у групі жіночої статі (група А1) свідчать про їх меншу схильність до розладів порівняно із особами чоловічої статі (група А2) на ранніх (І-ІІ) стадіях ВІЛ-інфекції. На пізніших стадіях (ІІІ- IV) виявлено, що жінки мали виражені тривожні та депресивні порушення (група B1), тоді як у чоловіків виявлено ознаки когнітивних та депресивних розладів (група B2).

**Ключові слова:** нейроСНІД, діагностика, тестування, здоров'я, соціум.

**Автор, відповідальний за листування:** Дмитро Сосновенко, Сумський державний університет, кафедра інфекційних хвороб з епідеміологією; e-mail: <u>d.sosnovenko@kinf.sumdu.edu.ua</u>

#### INTRODUCTION / BCTYII

In-depth study of the pathogenesis of neuroAIDS allows for a better understanding of the neurotropic properties of the retrovirus [1]. Cases of HIV-infection with atypical clinical symptoms are encountered in practice [2]. Further exploration clinical neuroimmunological aspects of retroviral diseases confirms fundamental data regarding the accumulation and latent storage of viral material in cells of the central nervous system (CNS) and the gradual pathological impact on the biochemical reactions of the brain. This may be a cause of disturbances in the cognitive and psychic status of an individual, even in cases where the patient receives antiretroviral therapy (ART) while adhering to all treatment requirements and compliance [3].

Anxiety-depressive and cognitive disorders are observed more frequently in HIV-positive individuals (61.5%) compared to the HIV-negative population In addition to the direct impact of the retrovirus, other causes of such disorders may include a high level of susceptibility to stressful situations, decreased social support, lifelong dependence on ART within the studied cohort, and so forth [4, 5]. The presence of other mental disorders in the patient's medical history, CNS injuries, chronic and acute illnesses of various etiologies, use of narcotic substances and alcohol consumption, as well as the safety and well-being of the surrounding environment (military conflicts, natural disasters, economic and social status overall), play a crucial role in the diagnosis of neurocognitive and anxiety-depressive disorders [6-9]. Inadequately chosen therapy and insufficient patient discipline in adhering to treatment recommendations and disease control can have a significant impact on the emergence of any symptoms [10].

Despite the clear recommendations provided by the European AIDS Clinical Society (EACS) regarding the comprehensive examination of individuals with suspected HIV infection and their subsequent monitoring [11], many healthcare professionals and researchers assess only specific indicators of depression or anxiety [12]. It is important to consider the possibility of assessing cognitive status, other laboratory data, and

historical facts, which collectively can be informative for both early diagnosis and monitoring the effectiveness of therapy in HIV-positive individuals during outpatient treatment [1, 3, 13].

In general, these statements may provide novel insights for the diagnosis and monitoring of HIV-infected patients, emphasizing the importance of a comprehensive approach to assessing their condition.

#### MATERIALS AND METHODS

observational cross-sectional study conducted for this research project from 2019 to 2021. During this period, 121 HIV-positive individuals were examined at the State Institution "Regional Clinical Medical Center for Socially Dangerous Diseases" and at the State Institution "Medical Clinical Center for Infectious Diseases and Dermatovenerology named after Z. J. Krasovitsky". The diagnosis was confirmed the use of ELISA (Enzyme-Linked Immunosorbent Assay) and Western Blot testing, in compliance with the legislation of Ukraine. Epidemiological, clinical-anamnestic data, laboratory investigations were collected while adhering to all patient rights. The work was conducted in accordance with the requirements of the Helsinki Declaration. The criteria for selecting patients for inclusion in the research program were: HIV-positive status, receiving antiretroviral therapy (ART) for more than 6 months, adulthood, and the individual's voluntary consent to the processing of personal data and the results of laboratory and clinical studies. 50 individuals were excluded from the study due to the presence of exclusion criteria, namely: active alcohol and substance abuse, pregnancy, traumatic CNS injuries in the medical history, psychiatric disorders, adherence issues, experience in military events, lack of social support, unstable economic status; presence of acute illnesses or oncological conditions; engagement in a profession associated with high levels of psychological stress; advanced age. The study included 71 HIV-positive individuals who were undergoing outpatient treatment and had a compensated condition. The average age of the participants was  $37,7 (\pm 0,78)$  years. Of them, 41 were in stage I, 11 in stage II, 6 in stage III, and 13 in

stage IV of the clinical stage (ClSt) of the disease. Among them, there were 39 women with an average age of  $36.0~(\pm0.92)$  years and 32 men with an average age of  $39.8~(\pm1.24)$  years (Fig. 1). Among the probable transmission routes indicated by HIV-infected individuals, the sexual route predominated.

In 59 HIV-infected individuals, the viral load (VL) reached an undetectable level ≤40 RNA copies/mL of blood. In 12 individuals, the VL ranged from 102 to 202,967 RNA copies/mL of blood.

In 47 patients, a normal CD4 cell count (>500 cells/mL of blood) was observed, while 24 individuals had a reduced count (<500 cells/mL of blood) (Table 1).

From the time of establishing the HIV-positive status to the completion of observation, a change in ART regimen was implemented in 44 individuals. Thirty individuals in the treatment scheme were receiving efavirenz, azidothymidine (zidovudine), or had been treated with them earlier.

Table 1 – Clinical and laboratory characteristics of HIV-positive patients (individuals)

|  | Clinical stage, n |        |       |        |  |
|--|-------------------|--------|-------|--------|--|
| Index                                    | I                 | II     | III   | IV     |  |
|  | n = 41            | n = 11 | n = 6 | n = 13 |  |
| Subclinical anxiety disorders            | 20                | 2      | 2     | 7      |  |
| Subclinical depressive disorders         | 10                | 2      | 2     | 4      |  |
| Subclinical cognitive disorders          | 6                 | 2      | 2     | 7      |  |
| Clinikally expressed anxiety             | 6                 | 3      | 2     | 4      |  |
| Clinikally expressed depression          | 4                 | 2      | 1     | 4      |  |
| Clinikally expressed cognitive disorders | 5                 | 1      | 1     | 1      |  |
| VL level > 40 RNA copies/ml of blood     | 7                 | 0      | 1     | 4      |  |
| CD4 level < 500 copies/ml of blood       | 10                | 3      | 3     | 8      |  |

Notes. Expressed disorders were considered in the presence of clinical symptoms during examination and communication, confirmed by test results. Subclinical symptoms were considered based on corresponding test results without the presence of clinical symptoms

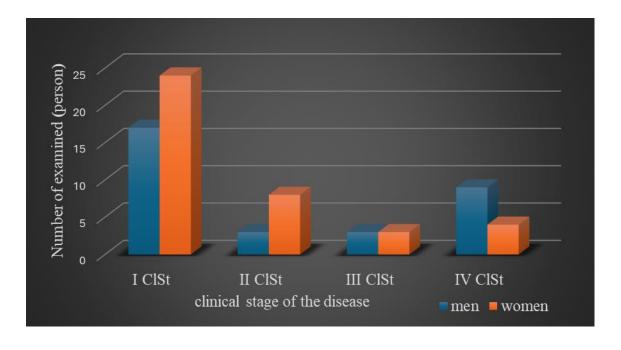


Figure 1 – Distribution by gender and clinical stage of HIV infection

With each patient, after obtaining voluntary consent, an interview was conducted, and documents were analyzed. Clinico-psychopathological and psychometric methods were used to diagnose neurocognitive and anxiety-depressive symptoms, patients were familiarized with the testing procedures, and scales such as the General Anxiety Disorder – 7 (GAD-7), The Hospital Anxiety and Depression Scale (HADS), and Mini-Mental State Examination (MMSE) were used in accordance with all criteria established by international consensus.

The MMSE scale was used to assess orientation in time and space, perception, concentration and counting, short-term memory, language, understanding, sequential action execution, and writing. The HADS scale was employed to assess the patient's level of anxiety (subscale A) and depression (subscale D) [14]. The GAD-7 scale was used to assess the level of anxiety and detect anxiety disorders, social phobias, and stress disorders.

The comparison group consisted of 43 clinically and mentally healthy HIV-negative individuals who were tested. The age of the group ranged from 20 to 68 years, with an average of  $29.5 \pm 1,68$  years.

Statistical data processing: Mathematical statistical methods were used. To determine the normality of distribution (for quantitative variables), the Shapiro-Wilk test was used. Two-way and multifactorial ANOVA tests were employed to check the validity of basic assumptions. Multiple comparisons and post hoc tests were used to identify significant differences between subgroups. In case of deviation from the basic hypothesis of equality of variances (Levene's test) and possible correlation between groups, the Student's t-test was utilized. Due to unequal variances in some groups, a more sensitive Welch's t-test was employed. The level of statistical significance during the verification of basic hypotheses was set at p < 0.05.

The information was processed using the computer programs Microsoft Office Excel 2010 and IBM SPSS Statistics v.23 (developer - IBM Corporation).

#### RESULTS

To study psychic and cognitive disorders at different clinical stages of HIV infection, four groups were created in the initial stage of the research. Group A included 41 individuals in CISt I (24 women and 17 men), with an average age of 37,0 (±1,15) years. Group B consisted of 11 individuals in CISt II (8 women and 3 men), with an age median of 34,0 and interquartile ranges (25-75) between 33,0 and 43,0; women were 1,3 times older than men. Group C consisted of 6 individuals in CISt III (3 women and 3 men), with an age ranging from 32 to 48 years (p = 0,965 according to Shapiro-Wilk), with an average of 39,3 (±2,36) years, and age did not depend on gender (p = 0,905 according to the t-test). Group D

consisted of 13 individuals in ClSt IV (4 women and 9 men), with an age range from 32 to 46 years (p = 0.947 according to Shapiro-Wilk), averaging 39,2 ( $\pm 4.53$ ) years, and age did not depend on gender (p = 0.314 according to the t-test) (Table 1).

In Group A (women and men, I ClSt), the obtained results coincided with HADS (A) and HADS (D) -6.1 points and were higher than in the control groups, by 1,8 and 1,4 times, respectively (p < 0.05). According to the GAD-7 scale, the average score was 2,2 times higher, and according to MMSE, it was 1,1 points lower than in the control groups (p < 0.05) (Table 2). The average duration of carrier status in the group was 4 years and 10 months.

In Group B (women and men II ClSt), according to the HADS (D) and GAD-7 scales, the scores were 2,1 and 2,4 times higher, respectively, and according to MMSE, it was 0,9 points lower compared to the control groups (p < 0,05) (Table 2). When comparing HADS (A) scores, no statistical significance was found. The average duration of carrier status in the group was 5 years and 3 months.

In Group C (women and men III ClSt), according to the HADS (A), HADS (D), and GAD-7 scales, the average scores were 1,7 and 2,4 times higher, and MMSE was 1,1 points lower compared to the control groups (p < 0,05) (Table 2). No statistical significance was found in the comparison of GAD-7 results. The average duration of carrier status in the group was 7 years and 1 month.

In Group D (women and men IV ClSt), according to the HADS (A), HADS (D), and GAD-7 scales, the scores were 1,7; 2,5, and 2,6 times higher, respectively, and according to the MMSE test, it was 1,8 points lower compared to the control groups. The results of the HADS (D) test were 1,3 times higher than in Group A (p < 0.05) (Table 2). The average duration of carrier status in the group was 7 years and 7 months.

14 individuals from Group A, 7 from Group B, 4 from Group C, and 7 from Group D were receiving efavirenz and/or zidovudine (azidothymidine) or had been treated with them in the past.

At the second stage, the dependence of changes between groups was assessed based on gender characteristics.

Group A1 consisted of 32 HIV-positive individuals of women gender in stages I and II, with an average age of 35,6 ( $\pm$ 1,08) years. Group A2 comprised men in stages I and II, with a total of 20 individuals and an average age of 39.7 ( $\pm$ 1.8) years. The average age of Group A2 was 4.1 years higher than that of Group A1 (p = 0.042 according to the t-Student test). Group B1 included 7 women in stages III and IV, with an average age of 38.0 ( $\pm$ 1.3) years. Group B2 comprised 12 men in stages III and IV, with an average age of 40.0 ( $\pm$ 1.5) years.

 $\begin{tabular}{ll} Table 2-Cognitive and anxiety-depressive disorders of HIV infection at different stages of the disease (average score) \end{tabular}$ 

| Scoring scale (in points) |    | Study group, n                          |                              |                               |                                     |                               |  |  |
|---------------------------|----|---|------------------------------|-------------------------------|-------------------------------------|-------------------------------|--|--|
|                           |    | Conparison (conditionally healthy n=43) | A (I – clinical stage, n=41) | B (II – clinical stage, n=11) | C<br>(III – clinical<br>stage, n=6) | D IV – (clinical stage, n=13) |  |  |
| GAD-7                     |    | 2,5(±0,6)                               | 5.7(±2,9)<br>b               | 6,1(±4,0)<br>c                | 7,8(±4,5)                           | 6,7(±3,7)<br>c                |  |  |
| HADS                      | D  | 3,3(±1,6)                               | 6,1(±3,3)<br>a               | 6,9(±2,9)<br>a                | 8,0(±2,5)<br>a                      | 8,3(±3,3)<br>a,d              |  |  |
|                           | Т  | 4,2(±1,1)                               | 6,1(±3,4)<br>a               | 6,4(±3,4)                     | 7,3(±2,6)<br>c                      | 7,3(±3,4)<br>a                |  |  |
| MM                        | SE | 29,7(±0,6)                              | 28,6(±2,0)<br>a              | 28,8(±1,4)<br>c               | 28,6(±1,3)<br>c                     | 27,9(±1,6)<br>a               |  |  |

Note: The base hypothesis of equality of variances is acceptable (p > 0.05), as assessed by Levene's test. When detecting intergroup effects, a two-way ANOVA (Analysis of Variance) was utilized. A significant difference was considered when  $p \le 0.05$ . For the indicators with a significant difference ( $p \le 0.05$ ), multiple comparisons and post hoc tests were conducted: a - Regarding the comparison group, there is a statistically significant difference ( $p \le 0.05$ ; p = 0.001, using Student's t-test). b - Concerning the comparison group, statistical significance of differences was confirmed ( $p \le 0.05$ ; using Welch's t-test). c - Regarding the comparison group, statistical significance of differences was established ( $p \le 0.05$ ; using Welch's t-test). d - For the HADS(D) test concerning Group A, statistical significance of differences was affirmed ( $p \le 0.05$ )

In group A1 (women I-II ClSt), the results of the HADS(T) test were 1.2 and 1.3 times higher than in the women and men control groups, respectively. The average values of the HADS(D) test were 1.8 and 1.7 times higher than in the women and men control groups, respectively. The results of the GAD-7 scale in group A1(women I-II ClSt) were 1.9 and 2.3 times higher than in the women and men control groups, respectively. The MMSE cognitive test results were 0.5 and 0.6 points lower than in the women and men control groups, respectively (p < 0.05) (Table 3). The average duration of carrier status in the group was 5 years and 2 months. Eleven patients were treated with efavirenz and/or azithromycin (zidovudine) or had received them in the past (Table 3).

The test results of HADS(T) and HADS(D) in group A2 (men I-II ClSt) were identical, being 1.5, 1.7, 2.1, and 2.0 times higher than the scores in the women and men control groups. Additionally, these scores were 1.25 and 1.2 times higher compared to the results of similar tests in group A1 (p < 0.05). The GAD-7 scores in group A2 were 2.2, 2.7, and 1.1 times higher compared to the men, women, and group A1, respectively (p < 0.05). In group A2 (men I-II ClSt), the results of the MMSE cognitive test were 1.8, 1.9, and 1.3 points lower than in the women, men, and group A1 control groups, respectively (p < 0.05) (Table 3). The

average duration of carrier status in the group was 4 years and 7 months. Eight patients received efavirenz and/or azithromycin (zidovudine) or had been treated with them in the past (Table 3).

In group B1 (women III-IV ClSt), the scores were found to be 1.9, 2.4, and 1.5 times higher than in the women, men control groups and group A1(women I-II ClSt), respectively. Regarding the HADS(D) scale, the scores were 2.5 and 2.3 times higher than in the women and men control groups, respectively. According to the GAD-7 scale, the average scores were 2.6 and 3.2 times higher than in the women and men control groups, respectively (p < 0.05) (Table 3). The MMSE scores did not differ from those of other groups. The average duration of carrier status was 6 years and 10 months. Four patients received efavirenz and/or azithromycin (zidovudine) or had been treated with them in the past.

In group B2 (men III-IV ClSt), the HADS(T) scale yielded an average score of 6.6 points; however, the comparison of the obtained results with other groups did not show a statistically significant difference. Scores on the HADS(D) scale were 2.5, 2.4, and 1.4 times higher than in the women, men, and group A1 (women I-II ClSt), control groups, respectively. The results of the GAD-7 test were 2.5 and 3.0 times higher than in the women and men control groups, respectively. MMSE testing scores were 2.2, 2.3, 1.7, and 2.0 points higher

than in the women, men control groups and A1 (women I-II ClSt), B1 (women III-IV ClSt), respectively (p < 0.05) (Table 3). The average duration of carrier status in the group was 7 years and 10 months. Seven patients received efavirenz and/or azithromycin (zidovudine) or had been treated with them in the past.

#### **DISCUSSION**

During the study of group A (women and men I ClSt), the observed changes were the smallest among all examined groups, except for the control group. This suggests a tendency towards stressful situations and a more stable emotional and cognitive state among patients in clinical stage I compared to all examined HIV-positive individuals, and less stability compared to HIV-negative individuals. In this group, a predominance

of subclinical anxiety-depressive symptoms over clinically pronounced symptoms was identified (p < 0,05) (Table 2). Among the pronounced clinical manifestations, increased nervous excitability, anxiety, and occasional cases of depressive disorders were diagnosed. The average duration of HIV infection in the group indicates that over 4 years and 10 months, individuals in this group develop a propensity for the gradual development of subclinical anxiety-depressive disorders. During the observation period, 34% of patients received potentially neurotoxic myelosuppressive drugs in their ART regimen, but no statistically significant correlation between clinical manifestations and their influence was confirmed.

Table 3 – Cognitive and anxiety-depressive manifestations of HIV infection by gender (in points)

|                                    |    | Study group, n                                |             |                         |                         |                           |                              |  |
|------------------------------------|----|---|-------------|-------------------------|-------------------------|---------------------------|------------------------------|--|
| Scoring<br>scale<br>(in<br>points) |    | Conparison<br>(conditionally healthy<br>n=43) |             | A1<br>(I, II – clinical | A2<br>(I, II – clinical | B1<br>(III, IV – clinical | B2<br>( III, IV –            |  |
|                                    |    | women<br>n=21                                 | men<br>n=22 | stage, women n=32)      | stage, men<br>n=20)     | stage, women<br>n=7)      | clinical stage,<br>men n=12) |  |
| GAD                                | -7 | 2,8(±3)                                       | 2,3(±0,3)   | 5,4(±3,7)<br>b, g       | 6,4(±0,8)<br>a, b       | 7,4(±1,1)<br>a, b         | 7,0(±1,4)<br>a, b            |  |
| HADS                               | D  | 3,2(±0,5)                                     | 3,4(±0,6)   | 5,8(±2,8)<br>a, e       | 7,0(±0,8)<br>a, b       | 8,1(±1,1)<br>a, b         | 8,3(±0,9)<br>a, b, f         |  |
|                                    | Т  | 4,4(±0,4)                                     | 4,1(±0,4)   | 5,6(±2,9)<br>e          | 7,0(±0,8)<br>b,         | 8,4(±1,3)<br>a, b, f      | 6,6(±0,8)                    |  |
| MM                                 | SE | 29,6(±0,1)                                    | 29,7(±0,1)  | 29,1(±0,1)<br>e, g      | 27,8(±0,5)<br>a, b, c   | 29,4(±0,7)                | 27,4(±0,3)<br>a, b, c, d     |  |

Note: Significant difference in indicators ( $p \le 0.05$  – multiple comparisons and a posteriori tests were used): a – relative to the comparison group of women; b – relative to the comparison group of men; c - in relation to group A1; d - in relation to group B1. There is a significant difference between the groups ( $p \le 0.05$ ; Student's t-test was used): e – in relation to the comparison group of men; f - in relation to group A1. g – relative to the women comparison group

The predisposition to depressive and anxiety disorders in individuals with clinical stage II (women and men of group B) did not statistically differ from those examined in clinical stage I, their condition significantly differed from the control group and a confident tendency toward gradual showed deterioration (p < 0.05) (Table 2). In this group, subclinical symptoms predominated, but among the individual pronounced symptoms were emotional fatigue, depression, and apathy. The average duration of infection was 5 years and 3 months, likely indicating further slow progression in line with the duration of the disease. During this period, 63% of individuals with clinical stage II received neurotoxic

myelosuppressive drugs, but no statistically significant correlation with their influence on clinical manifestations was confirmed.

In CISt III (women and men of group C), research results indicate more pronounced depressive and anxiety disorders in contrast to individuals in stages I and II (p < 0,05) (Table 2). Both subclinical and pronounced symptoms were identified in the group, including feelings of guilt, loss of sexual desire, and mood disorders. The average duration of the disease was 7 years and 1 month, indicating further progression of disorders. Sixty-six percent of individuals received neurotoxic and myelosuppressive drugs, but no statistical correlation with the disorders was established.

In individuals with CISt IV (women and men of group D), the indicators indicated a significant predisposition of group D to anxiety, depressive, and cognitive disorders. Pronounced depressive symptoms and anxiety dominated, reaching the highest levels among all those examined (p < 0.05) (Table 2). 53% of individuals received neurotoxic or myelosuppressive drugs, but no statistical correlation with disorders was established. The duration of the disease was 7 years and 7 months, indicating that the duration of HIV infection, a history of opportunistic infections, and prolonged ART use could significantly worsen cognitive and psychic functions of the central nervous system (p < 0.05) (Table 2).

The results of all tests for women with clinical stages I-II indicated an absence of a tendency towards disorders in all groups (p < 0.05) (Table 3).

#### CONCLUSIONS / BUCHOBKU

1. The least anxiety-depressive and cognitive disorders were found in people with the 1st stage of HIV infection, which indicates the stability of the emotional and cognitive state of patients at this stage. Individuals from II and III ClSt differed in a progressive tendency to anxiety and depressive disorders, demonstrating dependence on the stage of the disease. Patients with IV ClSt had the most pronounced anxiety,

The results of the studies in the men group with clinical stages I-II indicated a tendency towards anxiety-depressive disorders compared to females in the early stages of HIV (p < 0.05) (Table 3). Assessments of the results obtained in women with clinical stages III-IV indicated a greater predisposition in the later stages of the disease to anxiety-depressive disorders than individuals in the early stages of HIV infection (p < 0.05) (Table 3). Examined men with clinical stages III-IV showed the highest propensity, among all groups, for cognitive and depressive disorders. Signs of pronounced cognitive and depressive disorders were significantly more frequent in men compared to women in clinical stages I-IV (p < 0.05) (Table 3).

depressive and cognitive disorders, which may be related to the duration of HIV infection.

- 2. Women at early CISt are less prone to disorders compared to men. At later stages, women had more pronounced anxiety and depressive disorders, men showed signs of cognitive and depressive disorders.
- 3. The use of potentially neurotoxic drugs in patients did not indicate statistically significant changes in cognitive and psychosomatic functions.

#### PROSPECTS FOR FUTURE RESEARCH / ПЕРСПЕКТИВИ ПОДАЛЬШИХ ДОСЛІДЖЕНЬ

The study is an important contribution to the understanding of the relationships between HIV infection and psychic and cognitive aspects, and can also help in the development of individualized comprehensive approaches to the diagnosis and improvement of the condition of HIV-positive individuals with different stages of the disease.

#### AUTHOR CONTRIBUTIONS / ВКЛАД АВТОРІВ

Chemych M. D. - <u>0000-0002-7085-5448</u> <sup>1,2,3,4</sup> Sosnovenko D.S. - <u>0009-0008-1069-7530</u> <sup>1,2,3,4</sup>

- 1. A significant contribution to the design or construction of the manuscript; acquisition, analysis, or interpretation of data for the manuscript;
  - 2. Compilation of the manuscript or critical revision of its important intellectual content;
  - 3. Final approval of the version to be published;
- 4. Agree to be responsible for all aspects of the work, ensuring proper investigation and resolution of issues related to the accuracy or integrity of any part of the work.

#### FUNDING / ДЖЕРЕЛА ФІНАНСУВАННЯ

None.

#### CONFLICT OF INTEREST / KOHФЛІКТ ІНТЕРЕСІВ

The authors declare no conflict of interest.

#### REFERENCES/СПИСОК ЛІТЕРАТУРИ

1. Sosnovenko DS, Chemych OM, Chemych MD. Clinical and pathogenetic features of damage to the nervous

system at the initial clinical stages of HIV-infection [Kliniko-patohenetychni osoblyvosti urazhennia

- nervovoi systemy na pochatkovykh klinichnykh stadiiakh vil-infektsii]. *Infektsiyni khvoroby*. 2023(4):72-77. (in Ukrainian). DOI: https://doi.org/10.11603/1681-2727.2022.4.13705.
- Ances BM, Letendre SL. CROI 2019: neurologic complications of HIV disease. *Top Antivir Med. 2019 Apr;27(1):26-33*. PMID: 31137000; PMCID: PMC6550359.
- 3. Chemych MD, Sosnovenko DS, Yanchuk SM. Neuroimmune changes in early diagnosis of HIV infection [Neiroimunni zminy v rannii diahnostytsi vilinfektsii]. *Інфекційні хвороби*, 2021. 3: 68–74. (in Ukrainian). DOI: https://doi.org/10.11603/1681-2727.2021.3.12497
- Turan B., Budhwani H., Fazeli P.L., Browning W.R., Raper J.L., Mugavero M.J., Turan J.M. How Does Stigma Affect People Living with HIV? The Mediating Roles of Internalized and Anticipated HIV Stigma in the Effects of Perceived Community Stigma on Health and Psychosocial Outcomes. AIDS Behav. 2017;21:283–291. DOI: https://doi.org/10.1007/s10461-016-1451-5.
- Chambers L.A., Rueda S., Baker D.N., Wilson M.G., Deutsch R., Raeifar E., Rourke S.B., Team T.S.R. Stigma, HIV and health: A qualitative synthesis. *BMC Public Health*. 2015;15:848. DOI: https://doi.org/10.1186/s12889-015-2197-0.
- Portilla I., Reus S., León R., van-der Hofstadt C., Sánchez J., López N., Boix V., Merino E., Portilla J. Neurocognitive Impairment in Well-Controlled HIV-Infected Patients: A Cross-Sectional Study. *AIDS Res. Hum.* Retrovir. 2019;35:634–641. DOI: <a href="https://doi.org/10.1089/aid.2018.0279">https://doi.org/10.1089/aid.2018.0279</a>.
- Jain N, Prasad S, Czárth ZC, Chodnekar SY, Mohan S, Savchenko E, Panag DS, Tanasov A, Betka MM, Platos E, Świątek D, Krygowska AM, Rozani S, Srivastava M, Evangelou K, Gristina KL, Bordeniuc A, Akbari AR, Jain S, Kostiks A, Reinis A. War Psychiatry: Identifying and Managing the Neuropsychiatric Consequences of Armed Conflicts. *J Prim Care Community Health*. 2022 Jan-Dec;13:21501319221106625. DOI: <a href="https://doi.org/10.1177/21501319221106625">https://doi.org/10.1177/21501319221106625</a>. PMID: 35726205; PMCID: PMC9218442.
- Mao W, Agyapong VIO. The Role of Social Determinants in Mental Health and Resilience After

Received 30.02.2024 Accepted 29.05.2024

- Disasters: Implications for Public Health Policy and Practice. *Front Public Health*. 2021 May 19;9:658528. DOI: <a href="https://doi.org/10.3389/fpubh.2021.658528">https://doi.org/10.3389/fpubh.2021.658528</a>. PMID: 34095062; PMCID: PMC8170026.
- Smith AB, Cook PF. Comorbid mental health disorders in persons living with HIV: Adherence to antiretroviral therapy. *Arch Psychiatr Nurs*. 2019 Aug;33(4):364-370. DOI: <a href="https://doi.org/10.1016/j.apnu.2019.04.008">https://doi.org/10.1016/j.apnu.2019.04.008</a>. Epub 2019 Apr 19. PMID: 31280781; PMCID: PMC6814186
- Wykowski J, Kemp CG, Velloza J, Rao D, Drain PK. Associations Between Anxiety and Adherence to Antiretroviral Medications in Low- and Middle-Income Countries: A Systematic Review and Meta-analysis. AIDS Behav. 2019 Aug;23(8):2059-2071. DOI: <a href="https://doi.org/10.1007/s10461-018-02390-8">https://doi.org/10.1007/s10461-018-02390-8</a>. PMID: 30659424; PMCID: PMC6639150.
- Fehr J., Nicca D., Langewitz W., Haerry D. Guidelines of European AIDS Clinical Society (EACS) [(accessed on 14 July 2020)];2018 Available online: <a href="https://www.eacsociety.org/files/2018\_guidelines-9.1-english.pdf">https://www.eacsociety.org/files/2018\_guidelines-9.1-english.pdf</a>
- For the Cognitive Impairment in People with HIV in the European Region (CIPHER) Study Group. Haddow L.J., Laverick R., Daskalopoulou M., McDonnell J., Lampe F.C., Gilson R., Speakman A., Antinori A., Balestra P., et al. Multicenter European Prevalence Study of Neurocognitive Impairment and Associated Factors in HIV Positive Patients. AIDS Behav. 2018;22:1573– 1583. DOI: https://doi.org/10.1007/s10461-017-1683-z.
- Chemych M, Sosnovenko D, Chemych O, Berest O. Hematological changes of endogenic intoxication, nonspecific reactivity and inflammation activity indices in hiv-infected patients. Wiadomosci Lekarskie, 2020;73(5):983-987. DOI: https://doi.org/10.36740/WLek202005127
- Portilla-Tamarit I, Ruiz-Robledillo N, Díez-Martínez M, Ferrer-Cascales R, Alcocer-Bruno C, Portilla J. The Role of Mental Health Conditions in the Diagnosis of Neurocognitive Impairment in People Living with HIV. *Diagnostics (Basel)*. 2020 Jul 30;10(8):543. DOI: <a href="https://doi.org/10.3390/diagnostics10080543">https://doi.org/10.3390/diagnostics10080543</a>. PMID: 32751759; PMCID: PMC7460528.

Одержано 30.02.2024 Затверджено до друку 29.05.2024

#### INFORMATION ABOUT THE AUTHORS / ВІДОМОСТІ ПРО АВТОРІВ

Chemych M. D. – MD, Professor, Sumy State University, Head of the Department of Infectious Diseases with Epidemiology; e-mail: <a href="mailto:n.chemych@kinf.sumdu.edu.ua">n.chemych@kinf.sumdu.edu.ua</a>

ORCID ID: https://orcid.org/0000-0002-7085-5448

Sosnovenko D. S. Postgraduate student of Department of Infectious Diseases with Epidemiology, Sumy State University; e-mail: <a href="mailto:d.sosnovenko@kinf.sumdu.edu.ua">d.sosnovenko@kinf.sumdu.edu.ua</a>

ORCID ID: https://orcid.org/0000-0001-6632-0603