

ANALYSIS OF IMMUNOLOGICAL AND VIROLOGICAL RESPONSE IN HIV-POSITIVE PATIENTS DEPENDING ON THE TIME OF DETECTION OF HIV-INFECTION

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Abstract. ART decreases the viral load to a minimum level and retains this level for a long time, however, an increase in the number of CD4 lymphocytes is not always determined, which indicates the lack of immunological success of ART. Despite the long-term use of ART, this category of patients retains an immunodeficiency state and, as a result, an increased risk of the onset of AIDS.

Methods. Retrospective study of the outpatient cards, which include 455 HIV-positive patients registered at the Republican AIDS Center and receiving ART on different periods of the disease was carried out. In all patients, the diagnosis was confirmed clinically and laboratory by ELISA and immunoblotting.

Results. The average age of the examined patients was 42.2 years. The duration of the disease in patients after the detection of HIV before the initiation of ART is 1 to 16 years. The virological response after three years of receiving ART was manifested by a decrease in the viral load below 500 copies of RNA in most HIV-infected patients (90%) and was absent only in 10%. The best result was in the group with initially higher CD4 counts. The initial level of CD4-lymphocytes before starting ART did not influence on the increase in the level of CD4-lymphocytes. Comorbid conditions and somatic pathology affect virological and immunological efficacy.

Conclusion. The data obtained make it possible to reveal in a new way the relationship of clinical manifestations with immunological manifestations, to facilitate the diagnosis and therapy of the disease. Comorbid conditions and somatic pathology affect both virological and immunological effectiveness. The initial level of CD4-lymphocytes before starting ART did not influence on the increase in the level of CD4-lymphocytes, but it affect the virological response.

Keywords: HIV-infection, CD4-lymphocytes, viral load, antiretroviral therapy (ART)

Infectious diseases have always been a serious problem of global health. Infections prone to epidemic spread are a serious public health concern in all countries. HIV-infection affects all medical social aspects. Lack of exact influence of the efforts made on the final result requires clarifying the reasons and making decisions to adjust the strategy and tactics of combating the HIV epidemic, taking into account the achievements of modern science. **Currently, clinical course of HIV-infection is characterized by a long-term period with possible various opportunistic infections and an increase in the number of concomitant diseases [10, 7-18; 5, 368] and comorbid conditions [8, 292-6]. Highly active antiretroviral therapy has increased both the duration and quality of life of HIV-positive patients. However, the use of ART has its own problems associated with side effects and the need for high adherence, which not everyone is able to comply with. Antiretroviral therapy decreases the viral load to a minimum level and keep this viral load level for a long time, however, an increase in the number of CD4 lymphocytes is not always determined [4, 152-160; 6, 1-5]. It shows the lack of immunological success of ART and an increase of mortality rate [7, 288-293]. Scientific literary data are rather contradictory on the factors of effectiveness and ineffectiveness of ART, the occurrence of comorbid conditions, complications, improvement in the condition of one patient and deterioration in another [1, 11-24]. Clinical research on improving the clinical condition and laboratory parameters, identifying factors influencing on the effectiveness of ART remain relevant both in practical and theoretical aspects.**

Purpose. To study the peculiarities of changes and relationship of the virological and immunological response to ART in HIV-positive patients.

Material and methods. Retrospective study of the outpatient cards, which include 455 HIV-positive patients registered at the Republican AIDS Center and receiving ART on different periods of the disease was carried out. All the patients were registered at the Republican AIDS Center with the diagnosis that was clinically and laboratory confirmed

by ELISA and immunoblot methods. 237 (52%) patients are female, 218 (48%) are male. All patients were observed by infectious disease doctors and consulted by other specialists. The results of analyzes of CD4 lymphocytes and viral load for different years were analyzed. HIV-infection was diagnosed and prescriptions of ART were carried out in accordance with the national clinical protocols on HIV infection. Clinical stage of HIV infection, number of CD4 lymphocytes, AIDS indicator and concomitant diseases were taken into account. The analysis of the level of immune deficiency before the initiation of ART and in the dynamics of treatment after 3 years was carried out.

The results were statistically processed by using standard statistics methods using MS Excel 2007.

Results and discussion. Patients were divided into groups depending on the level of CD4-lymphocytes at the time of initiation of ART: with CD4-lymphocyte level less than 50 cells / μL , from 50 to 100 cells / μL , from 100 to 200 cells / μL , from 200 up to 350 cells / μL and CD4- lymphocytes more than 350 cells / μL (Fig. 1). The average age of the examined persons was 42 years. After HIV-infection is detected the average duration of the course of the disease in patients before starting ART was from 1 to 16 years.

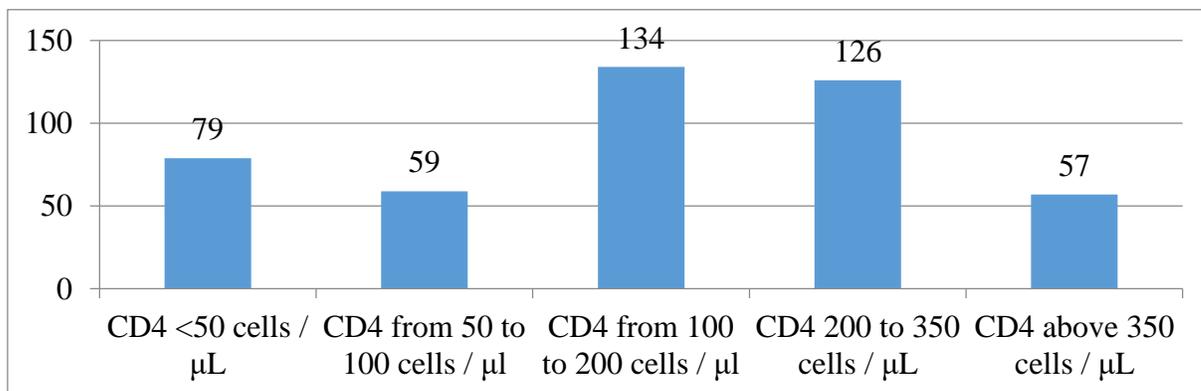


Fig. 1. Distribution of patients depending on the level of CD4 lymphocytes

The number of newly diagnosed patients at the time of ART prescription was 226 (49.6%), who were prescribed ART immediately after diagnosis. 25 HIV-infected patients were on the first stage, which was 5.5% of the total number of patients observed. 81 (18%) patients are on the second stage. The largest number of patients - 243 (53.5%) were on the third stage and 86 (23%) patients were at the fourth stage of HIV-infection (Fig. 2). Virological response with a decrease in viral load (VL) below 500 RNA copies / ml was found in the majority of HIV-positive patients (90%), and only in 10% it was absent. After three years after prescription of ART, depending on the initial CD4 lymphocyte counts, it was found that in the group of patients with CD4 lymphocytes below 50 cells / μL , viral load decrease less than 500 RNA copies / ml was observed in all patients, except one patient (diagnosis: HIV infection. Clinical stage 3, weight loss of more than 10%, unexplained prolonged fever, diarrhea for more than 2 months, aphthous stomatitis, herpes zoster(date: 09/14/2015, HSV: 02/26/2016) with viral load of 10 217 RNA copies / ml three years after receiving ART.

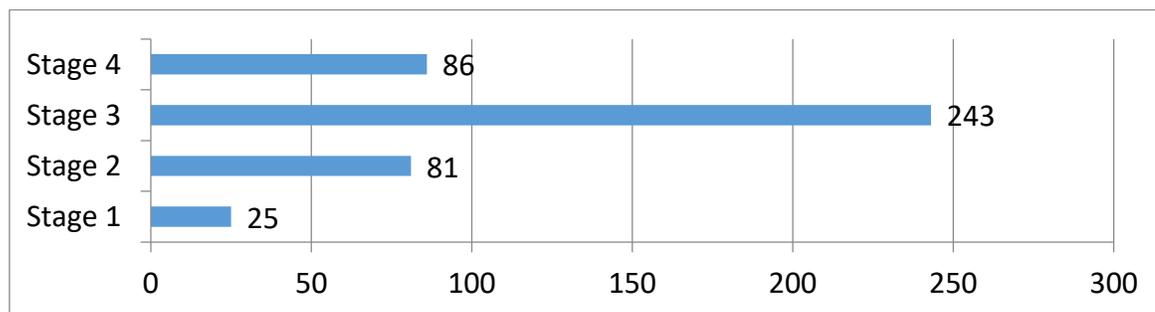


Fig. 2. Number of examined patients on different clinical stages (N=455)

All patients in the group of patients with CD4 lymphocytes from 50 cells / μL to 100 showed a decrease in viral load, only in one patient it remained high and amounted to 1 386 386 RNA copies / ml. Among the group of patients with initial CD4 lymphocyte counts from 100 to 200 cells / μL , viral load remained high in 5 patients. In the group of patients with CD4 lymphocytes from 200 to 350 cells / μL at the beginning of ART, the viral load became less than 500 RNA copies / ml in all patients (100%). The time point of HIV-infection detection did not influence on the virological response.

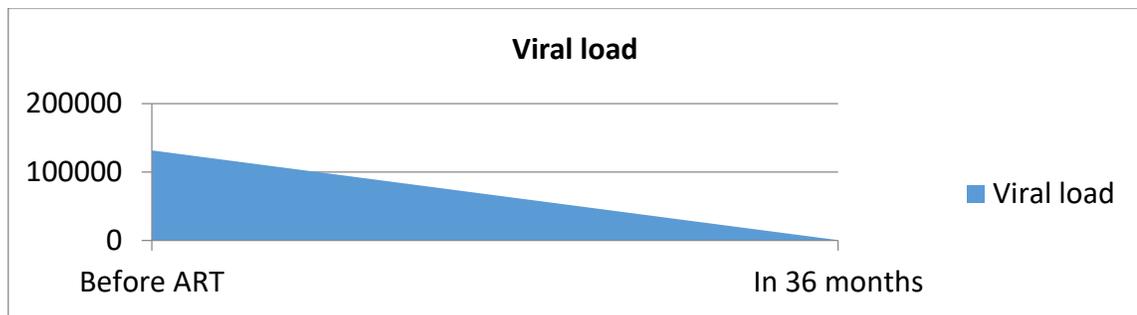


Fig. 3. Trends in viral load during ART

The initial level of CD4 lymphocytes of the general group of HIV-positive patients before starting ART was 196.97 cells / μ L. After 3 years of the start of ART, CD4 lymphocytes increased to 375.57 cells / μ L. When analyzed by groups depending on CD4, it was revealed that in group 1 with CD4 lymphocytes below 50 cells / μ L, after 3 years of ART, CD4 lymphocytes increased to 297 cells / μ L (initial - 27 cells / μ L), which showed an increase of 11 times. In group 2 with CD4 lymphocytes from 50 to 100 cells / μ L, the number of lymphocytes increased 3 times, which amounted to 229.3 cells / μ L (initial-74 cells / μ L). In the group with CD4 lymphocytes from 100 to 200 cells / μ L, the number of CD4 lymphocytes increased by 1.5, up to 418.6 cells / μ L (initial - 269 cells / μ L). In the group with CD4 lymphocytes from 200 to 350 cells / μ L, the number of CD4 lymphocytes increased 1.5 times (it reached 612.8 cells / μ L, with an initial count of 403.8 cells / μ L).

Among the group of patients with initial CD4-lymphocyte counts 100 to 200 cells / μ L, the viral load remained high in 5 patients, of which three were on the third stage with diagnoses: HIV infection, clinical stage 3, body weight loss of more than 10%, unexplained long-term fever, diarrhea for more than 2 months, aphthous stomatitis, herpes zoster (date: 09/14/2015), HSV (date: 02/26/2016) (Viral load - 871 RNA copies).

The second patient with diagnosis: HIV infection, clinical stage 3, recurrent infections of the upper respiratory tract, persistent generalized lymphadenopathy, weight loss up to 10%, candidal stomatitis, gingivitis, unexplained diarrhea for more than 1 month, tuberculosis of the middle lobe of the right lung (09/08/2016), remission (09/16/2016) on ART 02.2017, 10.2017, 03.2019 (VL -787 RNA copies).

The third patient with VL-1027 RNA copies, diagnosis: HIV infection, stage 3, recurrent candidiasis stomatitis, recurrent upper respiratory tract infections, weight loss up to 10% (08/12/2015), remission on ART 10.2016, 07.2017, 11.2018, 04.2019

One patient was at the second stage of HIV infection, clinical stage 2, persistent generalized lymphadenopathy, recurrent upper respiratory tract infection, angular cheilitis (12.2015), remission on ART 04.2017, 04.2018, 11..2019, VL-13563 copies of RNA. Also, one patient was at the first stage of HIV-infection, clinical stage 1, asymptomatic (12.12.2015), persistent generalized lymphadenopathy (17.01.2018), but VL-1090 RNA copies and remained high after 3 years of ART.

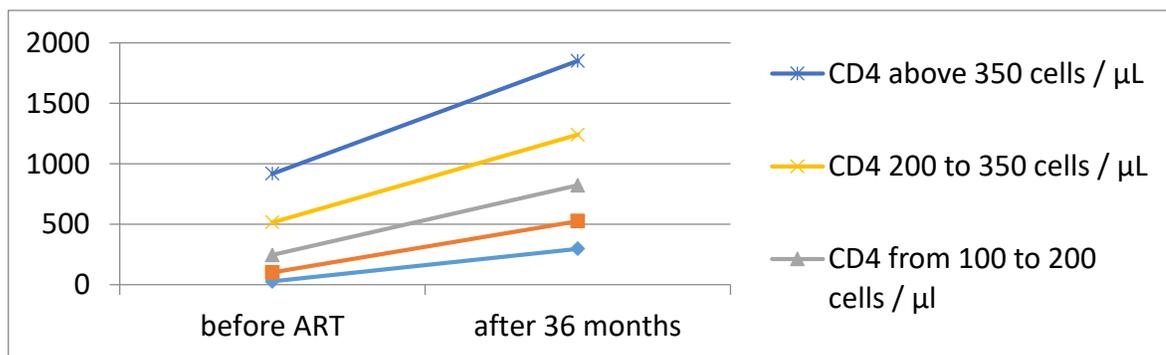


Fig. 4. Dynamics of the number of CD4 lymphocytes on ART

When dividing the general group of patients into two groups of ART initiation: patients with duration of HIV-infection of 6-15 years and those who started ART therapy immediately upon detection of HIV, it turned out that no significant difference was found.

Analysis of opportunistic and concomitant diseases in the study group of patients found that 72.3% of patients had several comorbid conditions at once. Diseases of the gastrointestinal tract manifested in the form of chronic diarrhea of unknown etiology in 10% patients, angular cheilitis in 1.6%, candidal lesions of the mucous membranes of the oral cavity and esophagus in 28%, weight loss of more than 10% was in 18.75% and cachexia in 2,8% respectively. Among the most

common pathologies of the gastrointestinal tract, the following diseases were identified: chronic gastroduodenitis 48%, pancreatitis of various genesis 22%, cholecystitis 55%, duodenal ulcer 8%. In 92% of cases, several pathologies were simultaneously noted in the same patient. Among the examined patients, chronic viral hepatitis was diagnosed in 23 (6.5%) patients, including 16 (4.54%) HCV and 7 (1.9%) HBV respectively. In addition, among the patients, essential hypertension was detected in 5.49%, lupus erythematosus in 1 patient.

The immunological efficacy of ART is influenced by various factors [18,19,20], the main of which are various comorbid conditions, concomitant pathology, which was confirmed in our studies and is consistent with literature data [3, 434-437]. The data on the starting level of CD4 lymphocytes are extremely contradictory [2, 942-947], according to the data of Oleynik A.F., Fazylov V.Kh. an initially low level of CD4-lymphocytes is probably the most unfavorable in relation to the increase of CD4-lymphocytes with ART [9, 114-119], however, when analyzing our results, in the group with an initially low level of CD4-lymphocytes there was an 11-fold increase in results. However, in group 5 with higher levels of CD4 lymphocytes, an increase was observed only 1.5 times.

Conclusion.

1. The duration of HIV-infection prior to initiation of ART does not influence on the virological efficacy of the therapy.

2. Patients, who initially had several concomitant diseases and comorbid conditions, showed the worst immunological and virological efficacy of ART.

3. The CD4-lymphocyte count before starting ART influences on virological efficacy.

4. The virological response in not all HIV-positive patients correlated with the immunological response, which was due to the number of comorbid conditions, the time of initiation of the therapy, and the starting level of CD4-lymphocytes.

The study allows to reveal the relationship of clinical manifestations with immunological ones in a new way and contribute to a different approach to the diagnosis and therapy of HIV-infection.

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