

GEORGIAN MEDICAL NEWS

ISSN 1512-0112

No 1 (322) Январь 2022

ТБИЛИСИ - NEW YORK



ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии
საქართველოს სამედიცინო სიახლენი

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CLINICAL AND HAEMATOLOGICAL CHANGES AMONG HIV PATIENTS

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Anemia is a clinical and hematological condition that is caused by decrease of red blood cell count and/or hemoglobin decrease in a unit of blood volume. It is characterized by abnormalities of oxygen transport with respective consequences [1].

A considerable part of pathology in red blood cells, white blood cells, platelets and clotting factors is associated with systematic diseases [2]. Anemia of chronic diseases (ACD) occurs in patients with chronic systematic pathologies. HIV/AIDS are often in the list of chronic systemic diseases that most often lead to ACD as well as a number of states which are often combined with immunodeficiency caused by HIV worsening the course of the illness. They are tuberculosis, chronic infections of urinary tract, multiple bronchiectasis, chronic abscesses, osteomyelitis, infective endocarditis, inflammatory diseases of gastrointestinal tract, thrombophlebitis, malignant tumors including lymphomas, pathology of cardiovascular system, etc. [2].

ACD is often normochromic, sometimes slightly hypochromic. This type of anemia usually has moderately expressed character (meaning that Hb concentration in peripheral blood is more than 90 g/l). The severity of CDA correlates with the severity of the main course of disease [2].

Iron concentration in blood serum and iron-binding capacity usually decrease iron capacity when ACD develops. In this case the amount of ferritin in serum is regular or slightly increased. Iron storage in the bone marrow does not change, but the result shading erythroblasts in iron is negative [2].

Pathogenesis of ACD is based on the amount of changes that accompany chronic systemic diseases. For example, the hept-sydn, produced by the liver during inflammatory processes in response to stimulation by cytokines, inhibits iron absorption and its release from macrophages in blood plasma. Excess levels of cytokines like IL-1, IL-6, TNF and γ -interferon influence on macrophage and red blood cells progenitor in bone marrow. As a result, erythropoiesis weakens, the ability of bone marrow to utilize iron decreases and the sensitivity of erythrocyte lineage cells to erythropoietins reduces [2].

G.S. Surzykova and coauthors [3] also indicate that increased levels of proinflammatory cytokines as TNF- α , IL-1 and IL-6 promote the development of ACD. On the other hand, a number of foreign scientists point to the increase of concentrations of TNF- α in biological fluids of HIV-positive patients, particularly in association with inflammatory changes in periodontal tissues [4-6]. It also coincides with the results of our studies, which have found a significant increase in TNF- α concentration in oral liquid of HIV-infected patients [7,8].

While treating ACD, specialists come to the idea that the main chronic disease must be treated first. But when it comes to HIV/AIDS, the best result with ACD therapy can be considered to maintain normal function of red blood cells [2].

The aim of our study was to investigate the nature of red blood cells changes in patients with HIV infection, to identify features of ACD in this group of patients, and to establish connection between changes in oral cavity and peripheral blood parameters.

Material and methods. 94 HIV-patients, who were subjects to regular medical check-up in Poltava Regional Center for AIDS Prevention and Control, took part in the study. There were

58 women and 36 men registered for the survey. The age of the patients ranged from 20 to 49 years.

The investigation of dental status in HIV-infected patients was performed with the help of generally accepted criteria. The survey was conducted in the morning when there was natural lightning in an in-patient dentist's surgery. The personal protective equipment, medical clothes and a cap, a mask, glasses and rubber gloves were used during the work with patients.

While making a diagnosis, anamnestic, clinical, partly radiographic criteria and data of oral cavity index assessment were taken into consideration.

First, an application form including patient's name, age, nationality and profession was taken and worked out. Secondly, attention was paid to patients' complaints. Then, the conditions of face and neck skin, visible mucous membranes of the nose and eyes, maxillofacial lymph nodes and trigeminal nerve exit points were determined. Vermilion border was examined twice: with the mouth closed and open. The examination of oral cavity was performed with a wide open mouth. The conditions of mucosa membrane, tongue, salivary glands, dentitions, occlusion and the presence of tooth-jaw anomalies were determined. The usage of dentures in the patients and the necessity of them were also recorded.

The condition of hard tooth tissues was evaluated according to the main clinical methods such as inspection, probing, percussion, palpation and termo-diagnostic. X-ray examination was used as one of additional research method. The presence of non-carious dental traumas, prevalence and intensity of caries (CPE) were determined [9].

The diagnosis of periodontal tissue diseases was made according to the classification by M.F. Danylevskiy [10]. Inflammation in the gums was evaluated for the presence of gum discoloration (redness), changes of their topography (edema) and consistency (pastoznost). The presence of bleeding, ulceration, hypertrophic and atrophic processes, the appearance of gingival and periodontal pockets and the value of epithelial junction loss were estimated. The attention was paid to the presence of purulent exudate and tooth mobility. The degree of bone tissue destruction was evaluated according to the X-ray pictures. In some cases, a formalin test was used [11].

To evaluate the oral hygiene condition, the simplified oral hygiene index by J.C.Green and J.R.Vermillion (OHI-S, Oral Hygiene Index Simplified, Green-Vermillion, 1964) was used [9-11]. It is appropriate for the examination of a large number of people [10,13].

Quantitative assessment of periodontal status was performed with the help of special indices, which convert in objective data and transfer to a numerical interpretation the extent of destruction and gums inflammation. The indices based on literature data and information on the objectivity reproducible parameters were chosen [9,11-13]. Papillae bleeding index (PBI) by Saxer and Muhlemann [9,14], papillary-marginally-alveolar index PMA modified by Parma [9,10,15], complex periodontal index (CPI) [9,11] and periodontal index (PDI) by Ramfjord [20] were applied. Qualitative assessment of periodontal status was performed using samples by Schiller-Pisarev and interpreted in numerical version by Svrakov [18].

The conditions of oral mucosa and vermilion border were evaluated visually. Herewith, the attention was paid to its color, texture, shape and integrity. If there were some pathological elements in the mucosa membrane, their size, shape, response to mechanical stimuli and bleeding was determined. Diagnosis of oral mucosa diseases was performed according to the classification by Y.V. Borovskiy, A.L. Mashkyleyson (1984).

Laboratory studies of peripheral blood were conducted for 90 patients. For this purpose the hematology analyzer from centralized diagnostic laboratory of Poltava's regional center of HIV infection and AIDS and other laboratories according to patients' places of living were used.

Some parameters as RBC (red blood cells), HGB (hemoglobin), HCT (hematocrit) were analyzed. Parameters which characterize the erythrocyte morphology: mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) were also studied. The erythrocyte anisocytosis index like red cell distribution width (RDW) was analyzed too.

For nonparametric (semi quantitative and qualitative) indicators the U Mann-Whitney and Kruskal-Wallis criterion were calculated [21,22]. For analyzing the relationships between the quantitative parameters we determined the Pearson correlation coefficient [22].

Results and Discussion. During the examination of the face and oral cavity in HIV- patients, a special attention was paid to the clinical implications of anemia.

During the examination of the face and neck it was found that 19 HIV-patients (20.21%) had pale skin, 44 individuals (46.81%) had the elements of damaged skin, mostly in the form of spots (32.98% of cases), seals (18.09% of cases) and squamas (11.7% of cases).

22 HIV-infected people (23.4% of cases) had the pale colour of vermilion border. 5 HIV patients (5.32% of cases) had swollen lips and 46 (48.9% of cases) – dry lips. 31 (32.98% of cases) and 12 (12.77% of cases) patients with HIV status had vermilion border squamas and cracks, respectively. These elements are caused by lips dryness and are clinical manifestations of anemic blood changes.

The examination of HIV patient's oral cavity showed that 3 persons (3.19% of cases) had pallor and 19 individuals (20.21% of cases) dryness in the mucous membrane. 61 HIV patients had elements of oral lesion (64.89% of cases). The most common cases were injected vessels (28.72% of cases), petechiae (22.34%), granulation (9,57%), plaque (9,57%), induration (8.51%) and spots (7.45%). Less commonly observed cases were erosion (5.32% of cases), ulceration (2.13%) and patch (1.06%).

The analysis of the tongue condition of HIV-infected individuals showed that 63 patients (67.02% of cases) had edema, 72 patients (76.6% of cases) – the presence of lesions. 5 people (5.32% of cases) had the atrophy of tongue papillae, which is a clinical sign of anemia.

The investigation of major salivary glands in HIV-infected persons revealed that 1 patient (1.06% of cases) had pale skin and pallor in mucosa in the area of parotid glands. One patient (1.06% of cases) felt pain while palpating the right mandibular salivary gland. 2 patients (2.13% of cases) had an increase of major salivary glands density. 22 patients (23.4%) had secretion changes: 19 individuals (20.21% of cases) suf-

fered from reduced secretion and 3 patients (3.19%) – from increased secretion.

During the primary analysis of surveyed HIV-patients, 48 patients (53.33%) had reduction in the number of red blood cells, which was regarded as a sign of anemia of chronic diseases (ACD). None of the surveyed was found with polycythemia. However, only 5 people (5.56% of patients) with MCH index indicated hypochromic anemia, and 29 patients (32.22%) had signs of hyperchromic anemia. Increasing MCH index - average hemoglobin in one erythrocyte - may indicate organic liver damage [16]. Since, 27 HIV-patients (28.72%) with chronic hepatitis type C and 3 people (3.19% of patients) with chronic viral hepatitis type B + C were revealed, it became clear that there would be signs of hyperchromic anemia alongside with hepatobiliary system involvement.

Only 25 patients (27.78% of surveyed people) had hemoglobin concentration below generally accepted norms, but no patients with HIV were found to have hemoglobin concentration less than 90 g/L. It indicates averagely expressed ACD associated with HIV infection. These results coincide with data by Atul B. Mehta, A. Victor Hoffbrand, who also pointed to averagely expressed CDA as a rule [2].

Hematocrit (HCT) shows the volume fraction of red blood cells in whole blood and depends on their number and volume. Among surveyed people 21 individuals (27.78% of patients) had low level of hematocrit that indicated the resessing symptoms of anemia. Only 3 persons (3.33% of patients) had high level of hematocrit.

52 surveyed people (57.78% of patients) had the average volume of red blood cells - index MCV (mean corpuscular volume) - within normal limits and 38 individuals (42.22%) had this parameter changed. 8 HIV-positive patients (8,89% of surveyed people) had MCV below than normal, and 30 patients (33.33%), had this parameter more than normal values. Index MCV can be used to determine violations of water-electrolyte metabolism. Higher level of this parameter indicates hypotonic violations and lower level - hypertensive changes. In addition, increased mean corpuscular volume also indicates concomitant liver disease [16]. It coincides with the fact that 31.91% of HIV-patients were found with organic changes in the liver, such as chronic viral hepatitis, in particular.

Analysis of mean corpuscular hemoglobin concentration, which characterizes the average concentration of hemoglobin in red blood cells and determines the saturation of red blood cells, showed that only 9 surveyed people (10% patients) had changes in this parameter. Whilst 5 people (5.56%) had MCHC index increased, 4 (4.44%) had it reduced. This index as well as previous changes may indicate water-electrolyte metabolism. High level of this parameter indicates hypotonic violations and low – hypertensive changes [16].

3 (3.33%) patients with HIV status had anisocytosis of erythrocytes (RDW - red cell distribution width) increased, and 15 surveyed people (16.67%) – decreased.

The problem of anemia in HIV-patients is complicated by the fact that the presence of changes in red blood terms creates difficulties in selecting schemes of antiretroviral therapy (ART) [17-20]. A highly active ART enhances changes in the blood. On this basis, the parameters of red blood cells in HIV-patients were analyzed according to taking highly active ART (Table 1).

Table 1. Changes of red blood parameters in HIV-positive people taking and not- taking highly active ART drugs

Parameter	HIV-infected patients who take highly active ART n=42	HIV-infected patients who don't take highly active ART n=48	p
RBC	3,76±0,08	4,28±0,08	<0,01
HGB	131,76±2,77	128,63±2,45	-
HCT	0,40±0,01	0,37±0,01	<0,05
MCV	105,36±2,17	87,69±1,33	<0,001
MCH	36,89±1,60	30,37±0,51	<0,001
MCHC	336,76±2,09	347,56±2,88	<0,01
RDV	11,12±0,29	12,00±0,28	<0,05

p - error probability according to Student's criterion

It was found that almost all the studied parameters except hemoglobin concentration were significantly different in HIV-positive patients taking and not-taking highly active ART drugs. Those patients, who have HIV-status and take highly active ART drugs, have significantly lower number of red blood cells, average hemoglobin level concentration and erythrocyte anisocytosis. On the other hand, the HIV patients on a specific antiviral treatment have such parameters as hematocrit, erythrocytes average volume and average hemoglobin in one erythrocyte significantly higher. These data show that taking highly active ART drugs really affects red blood cell count of HIV-infected patients and causes a disbalance of its indicators.

We analyzed the red blood parameters in patients with HIV infection, depending on the level of blood lymphocytes with CD4 cluster differentiation in plasmolemma. All investigations were divided into 3 groups: HIV-infected patients with a number of CD4-lymphocyte <200 cells in 1 mm³ of blood, that is below the critical level; patients with HIV status with a number of CD4-lymphocytes more than critical level, but less than normal (200-576 cells in 1 microliter of blood); patients with normal level of CD4-lymphocytes in the blood

associated with HIV infection. There weren't any significant changes in red blood parameters in HIV-patients found, depending on the level of lymphocytes with CD4 differentiation cluster in plasmolemma.

We also analyzed red blood parameters of surveyed HIV-infected patients, depending on the stage of the main disease. Taking into consideration the size of experimental groups, significant changes of indicators according to the Student's criterion were not found. But there was a distinct downward tendency in the number of red blood cells and hemoglobin (RBC indices and HGB) in peripheral blood of tested HIV-infected patients together with progression of the main disease. It was also seen an upward tendency in MCV parameter (average volume of red blood cells) in HIV-patient with deterioration of immunodeficiency condition.

The analysis of red blood parameters of HIV-patients depending on the state of periodontal tissues was also conducted. It was found that such indicators as HCT (hematocrit), MCHC (mean hemoglobin concentration) and RDV (anisocytosis index) increased significantly together with the progression of periodontal diseases. The relevant data are presented in Table 2.

Table 2. Red blood indicators of HIV-patients depending on the state of periodontal tissues

Parameter	HIV-patients with gingivitis n=5	HIV-patients with with generalized periodontitis internal severity n=7	HIV-patients with with generalized periodontitis I stage of severity n=29	HIV-patients with with generalized periodontitis II stage of severity n=27	HIV-patients with with generalized periodontitis III stage of severity n=21
RBC	3,95±0,29	3,99±0,19	4,20±0,13	3,95±0,12	3,96±0,11
HGB	129,20±6,42	127,71±6,52	134,52±3,27	126,45±3,85	129,38±3,16
HCT	0,36±0,01 ^{2,4}	0,38±0,01	0,40±0,01	0,38±0,02	0,39±0,01
MCV	93,20±6,90	94,57±4,80	95,86±3,82	96,74±3,39	95,76±3,22
MCH	32,98±1,61	32,84±1,62	32,31±0,81	32,76±1,15	36,04±3,12
MCHC	356,60±12,02	349,86±6,01	337,76±3,16 ⁴	339,59±3,58	347,76±3,17
RDV	11,40±0,70	11,54±0,50	11,09±0,30 ⁴	11,91±0,48	12,09±0,38

note: n - number of surveyed people; 1 – an error probability according to the Student's criterion <0.05 compared to peripheral blood of HIV-infected patients with generalized periodontitis initial severity;

2 – an error probability according to the Student's criterion <0.05 compared to peripheral blood of HIV-infected patients with generalized periodontitis I stage of severity;

3 – an error probability according to the Student's criterion <0.05 compared to peripheral blood of HIV-infected patients with generalized periodontitis II stage of severity;

4 – an error probability according to the Student's criterion <0.05 compared to peripheral blood of HIV-infected patients with generalized periodontitis III stage of severity

The results can be interesting in terms of identifying the pathogenic interactions in the development of inflammatory and degenerative changes in periodontal tissues and anemia of chronic disease associated with HIV infection.

Conclusion. Therefore, we can summarize the research. In the course of the study we identified clinical signs of anemia in maxillofacial area and oral cavity of HIV-infected people. 53.33% of the examined patients were found with the signs of anemia of chronic diseases in the clinical analysis of peripheral blood. During the analysis of red blood cell indicators in people with HIV a number of changes were observed. The problem of anemia in this group of patients was complicated by the taking of highly active ART. This circumstance makes blood changes deeper. It was revealed significant changes of red blood cells in people with HIV status, taking and not taking highly active ART. We also analyzed the studied parameters of red blood cells in patients with HIV infection, depending on the level of blood lymphocytes with CD4 cluster differentiation in plasmolemma, and depending on the stage of the main disease. We also analyzed and studied parameters depending on the state of periodontal tissues. Identified results can be interesting in terms of establishing pathogenesis relationships in developing inflammatory and degenerative changes in periodontal tissues and anemia of chronic diseases associated with HIV infection. These findings require further investigation and comprehensive analysis.

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SUMMARY

CLINICAL AND HAEMATOLOGICAL CHANGES AMONG HIV PATIENTS

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This is an article about anemia of chronic diseases in HIV patients. It follows a study of the nature of red blood cells changes in patients with HIV infection and the features of anemia of chronic diseases (ACD) in the particular group of patients. In addition, connection was established between changes in oral cavity and peripheral blood parameters.

The study identified clinical signs of anemia in maxillofacial area and oral cavity in HIV-infected people. During the analysis of red blood cell indicators in patients with HIV a number of changes were observed. The problem of anemia in this group was complicated by the patients taking highly active antiretroviral therapy (ART). The study revealed significant changes in red blood cell count in people with HIV status, who were either taking or not taking highly active ART. We also analyzed the studied parameters of red blood cells in patients with HIV infection, depending on level of blood lymphocytes with CD4 cluster differentiation in plasmolemma, and depending on the stage of the main disease. We also analyzed and studied parameters depending on the state of periodontal tissues. Identified results can be interesting in terms of establishing pathogenetical relationships in development of inflammatory and degenerative changes in periodontal tissues and anemia of chronic diseases associated with HIV infection. These findings require further investigation and more comprehensive analysis.

Keywords: HIV-infection, anemia, periodontal diseases, highly active antiretroviral therapy.

РЕЗЮМЕ

КЛИНИЧЕСКИЕ И ГЕМАТОЛОГИЧЕСКИЕ ИЗМЕНЕНИЯ У ВИЧ-ИНФИЦИРОВАННЫХ ПАЦИЕНТОВ

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В статье изучен характер гематологических изменений и особенности клинических признаков анемии в зависимости от нарушений элементов белой крови и состояния тканей пародонта у ВИЧ-инфицированных пациентов, леченных и нелеченных высокоактивными антиретровирусными препаратами.

В ходе исследования выявлены клинические признаки анемии в челюстно-лицевой области и полости рта пациентов со статусом ВИЧ. При анализе показателей красной крови у пациентов с ВИЧ-инфекцией отмечен ряд изменений. Проблема анемии среди этих пациентов осложнялась приемом высокоактивной антиретровирусной

терапии (АРТ). Установлены существенные изменения показателей эритроцитов у ВИЧ-инфицированных пациентов, принимавших и не принимавших АРТ, в зависимости от уровня лимфоцитов с кластерами дифференциации CD4 на плазмолеммах, стадии основного заболевания и состояния тканей пародонта. Выявленные результаты интересны с точки зрения установления патогенетических взаимосвязей в развитии воспалительных и дегенеративных изменений тканей пародонта и анемии хронических заболеваний на фоне ВИЧ-инфекции. Полученные результаты диктуют необходимость дальнейшего изучения и всестороннего анализа.

რეზიუმე

კლინიკური და ჰემატოლოგიური ცვლილებები აივ-ინფიცირებულ პაციენტებში

ნ.ილენკო-ლობაჩი, ტ.პეტრუშანკო, ნ.ილენკო, ო.ბოიჩენკო

პოლტავას სახელმწიფო სამედიცინო უნივერსიტეტი, უკრაინა

შესწავლილია ჰემატოლოგიური ცვლილებების ხასიათი და ანემიის კლინიკური ნიშნები თეთრი სისხლის ელემენტების დარღვევისა და პაროდონტის ქსოვილის მდგომარეობისგან დამოკიდებულებით მაღალაქტიური ანტივირუსული პრეპარატებით ნამკურნალებ და არანამკურნალებ აივ-ინფიცირებულ პაციენტებში.

კვლევის მსვლელობაში აივ-დაავადებულთა ყბასახის არეში და პირის ღრუში გამოვლინდა ანემიის კლინიკური ნიშნები. წითელი სისხლის მანკვებლების ანალიზმა გამოავლინა რიგი ცვლილებები. ანემიის განვითარება აღნიშნულ პაციენტებში გამოწვეული იყო მაღალაქტიური ანტივირუსული თერაპიის (ართ) გამოყენების შედეგად.

დადგენილია ერთროციტების მანკვებლების მნიშვნელოვანი ცვლილებები აივ-ინფიცირებულ პაციენტებში, რომლებსაც ჩაუტარდათ და არ ჩაუტარდათ ართ. მიღებული პარამეტრები გაანალიზებულია სისხლში ლიმფოციტების დონის CD4 დიფერენციაციის კლასტერებთან ერთად, ძირითად დაავადებისა და პაროდონტის ქსოვილების მდგომარეობის გათვალისწინებით. ჩატარებული კვლევის შედეგები საინტერესოა აივ-ინფექციის ფონზე ანემიის და პაროდონტის ქსოვილში დეგენერაციული ცვლილებების განვითარებაში პათოგენეტიკური ურთიერთკავშირის გამოვლენის თვალსაზრისით.