

## ORIGINAL ARTICLE

# HEMATOLOGICAL CHANGES OF ENDOGENIC INTOXICATION, NON-SPECIFIC REACTIVITY AND INFLAMMATION ACTIVITY INDICES IN HIV-INFECTED PATIENTS

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## ABSTRACT

**The aim:** To establish changes in hematological parameters of endogenous intoxication, nonspecific reactivity, activity of inflammation in HIV-infected persons, to improve verification of the clinical stage of the disease.

**Materials and methods:** Anamnestic, clinical, laboratory data. The statistical processing was performed in the Microsoft Office Excel 2010 and IBM SPSS Statistic 23 computer software, variational statistics processing (Student's t-criteria).

**Results:** 51 HIV-infected were examined (main group) and 44 clinically anamnestic healthy blood donors (comparison group). The study included 46 patients (5 were withdrawn due to failure to meet criteria – severe septic condition).

All patients were divided into three groups: A1 – all patients, 46 persons, men 76.0%, women – 24.0%; A2 – 11 people with I-III stages of HIV infection, men 72.7%, women – 27.3%; A3 – 35 HIV infected with stage IV disease, men 76.0%, women – 24.0%.

All patients had an increase in intoxication indices and sex-dependent changes.

Nonspecific reactivity indices in group A1 were above the norm, independent of gender except the index of neutrophils and lymphocyte (NLR). Below the norm is the immunoreactivity index (IR), the lymphocyte-monocyte ratio index (LMR), the lymphocyte index (lymph), the index of allergization (IA).

Indices of nonspecific reactivity of A2 patients exceeded the norm and were independent of sex, with the exception of IR, lymph, IA, which were reduced. Non-specific reactivity indices are increased in HIV-infected group A3. Below the norm were IR, LMR, lymph, IA.

Analyzing the activity indexes of inflammation, it became clear that the Krebs index (KI) was increased in all groups of patients; lymphocyte-granulocyte index (ILG) in groups A1 and A3 is less than normal, unlike patients in group A2, where it remained within the normal range. The leukocyte ratio and erythrocyte sedimentation rate (ILES) in A1 and A3 have increased rates, unlike in A2, where the index is smaller.

**Conclusions:** Men are predominantly HIV positive. The systemic immune response is more pronounced in women. There is a progressive impairment of immunological reactivity, indicating an immunodeficiency of the cell type with a decrease in nonspecific anti-infective protection. Patients with stage IV of HIV infection have moderate and severe inflammatory reactions, impaired reactivity, and are more pronounced in women.

**KEY WORDS:** HIV infection, integrative indicators, disease stages

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## INTRODUCTION

Blood cells are qualitatively and quantitatively interconnected with various tissues of the human body, having the ability to disrupt the constancy of the indicators and the normal ratio to each other, reflecting all physiological or pathophysiological processes of inflammatory, allergic, autoimmune or oncological genes [1, 2].

The pathogenesis of HIV infection is of great importance for the selectivity of the immune system virus, the main purpose of which is to protect the body from pathogenic infectious agents, and to ensure the equilibrium of the pathogenic microflora of the body [3].

Research of the development mechanism and pathological processes severity in various organs and tissues of the body using integrative hematologic parameters is a relevant topic of the current research for HIV.

## THE AIM

To establish changes in indicators of endogenous intoxication, nonspecific reactivity, activity of inflammation in HIV-infected at different stages of the disease and improve verification of the clinical stage of the disease.

## MATERIALS AND METHODS

51 HIV-infected were examined. Patients were mostly hospitalized (80%).

The criteria of involvement in the study was clearly confirmed and established the diagnosis of HIV. Exclusion criteria were: severe septic condition, autoimmune diseases. Five patients were removed from the study for non-compliance with the criteria.

Among the patients enrolled in the study were 35 men and 11 women, aged ( $40.75 \pm 1.21$ ) years. Of these, 3 people

with stage I HIV- infection, 2 with – II, 6 with – III and 35 with IV. The comparison group consisted of 44 clinically anamnestic healthy blood donors aged ( $37.95 \pm 1.72$ ) years.

It was performed: collecting of epidemiological, clinical and anamnestic data, clinical and laboratory studies. Using our developed Android mobile application [4], it was calculated integrative indicators of endogenous intoxication and immunoreactivity: leucocyte intoxication index (LII), hematological index of intoxication (HII), index of leucocytes shift (ISL), Krebs index (KI), immunoreactivity index (IR), lymphocyte-granulocyte index (ILG), neutrophil-lymphocyte ratio (NLR), lymphocyte-monocyte ratio (LMR), neutrophil reactive response (NRR), index of leukocyte and ESR ratio (ILES), lymphocyte index ( $I_{lymph}$ ), eosinophils-lymphocyte ratio (ELR), index of allergization (IA), nuclear index (NI), index of intoxication severity (IIS) [5,6].

The statistical processing was performed in the Microsoft Office Excel 2010 and IBM SPSS Statistic 23 computer software. Data were checked for group distribution normality using the Shapiro-Wilk statistics. In the groups of patients we used parametric methods because the obtained data conform the normal distribution – Student's t-test was used to analyze the quantitative data.

Present information about study design, applied methods and search of conflicts of interest when conceptualizing the data and before writing a final text of original article. Keeping a non-interventional nature of the presented work the appropriate anonymity and personal data processing were ethically verified according to the local hospital and the All-Ukrainian rules and orders. Basically, the Declaration of Helsinki (6th, rev., 2008, Seoul) and the Universal Declaration on Bioethics and Human Rights (2006) were a key documentation considering ethical decision making and conceptualization for the article's scientific content.

## RESULTS

All patients were divided into three groups: the first group (A1) included all HIV-infected persons – 46 persons, men were 76.0%, women – 24.0%, the average age was ( $40.75 \pm 1.21$ ) years; in the second (A2) group – 11 people with I – III stages of HIV infection, men 72.7%, women – 27.3%, aged ( $44.9 \pm 1.21$ ) years; in the third (A3) – 35 persons with stage IV disease only, men were 76.0%, women – 24.0%, age ( $39.6 \pm 1.31$ ) years.

In group A1, there was an increase in the index of intoxication compared to the norm – LII (by 2.0 times), ISL (by 1.7), HII (by 4.9), IIS (by 19.0), NRR (by 2.5). The dependence of indicators of HII, IIS, NRR on sex was found, in women they were higher than in men (respectively – in 2.2; 2.1; 1.2 times) ( $p < 0.05-0.001$ ) (Table 1).

Patients in the A2 group had similar changes, except for the IIS, which was above the norm by 25.0 times, and depending on the sex, the indicator was higher in women than in men by 2.7 times, and more than in the HIV-infected A1 groups by 1.3 times ( $p < 0.05-0.001$ ). Although NRR increased 1.4-fold and was sex-dependent (2.7-fold

higher in women than in men), it was 1.7-fold lower than in the A1 group ( $p < 0.05-0.001$ ).

Indicators of group A3 did not differ significantly from each other, did not depend on sex, except for HII and IIS, which increased by 5.0 and 17.8 times, respectively, depending on gender – exceeded for men, respectively – by 2.1 and 1.9 times ( $p < 0.05-0.001$ ).

Non-specific reactivity indices in group A1 were changed as follows: NLR, ELR, NI were above the norm, respectively – by 1.2, 1.2, 3.5 times ( $p < 0.05-0.001$ ). The changes did not depend on sex, except NLR in women which was higher by 1.6 than in men ( $p < 0.05-0.001$ ). Other indicators – IR, LMR,  $I_{lymph}$ , IA were below the norm, 1.1, 1.3, 1.4, 1.2 times ( $p < 0.05-0.001$ ), respectively, and did not depend on gender.

A2 patients indices of nonspecific reactivity: IR, LMR, ELR, NI, exceeded the norm by 1.1, 1.3, 1.2, 1.5 times respectively, and did not depend on sex, with the exception of IR, which was higher in men by 1.2 times more than women ( $p < 0.05-0.001$ ).  $I_{lymph}$  – below the norm by 1.1 times, regardless of gender ( $p < 0.05-0.001$ ). Normal level were LMR and IA. LMR and IA in women is 1.3 times lower than in men.

The non-specific reactivity index – NLR, ELR, and NI in HIV-infected group A3 increased by 1.2, 1.2, and 4.1 times, respectively ( $p < 0.05-0.001$ ). Were increased NLR (1.9 times), ELR (1.2 times) in women was more pronounced than in men ( $p < 0.05-0.001$ ). Below the norm, regardless of gender, in this group were IR (1.3), LMR (1.4),  $I_{lymph}$  (1.4), IA (1.3 times) ( $p < 0.05-0.001$ ).

Analyzing the indices of nonspecific reactivity it is established: NLR,  $I_{lymph}$ , ELR indices have no significant intergroup differences; IR, LMR, IA – have insignificant differences in groups A1 and A3. Comparing the data with the indicators of the A2 group, it is proved that the IR index is 1.3 and 1.4 times higher than in the A1 and A3 groups ( $p < 0.05-0.001$ ); LMR and IA within the normal range, but also more than 1.3 (A1), 1.4 (A3) times and 2.3, 2.7 times, respectively ( $p < 0.05-0.001$ ).

The analysis of inflammatory activity indices showed an increase in patients with A1 – KI, ILES (2.0 – 4.8 times) and gender dependence compared to normal, in women they are higher than in men (1.3 – 1.8 times) ( $p < 0.05-0.001$ ). ILG is 1.2 times less than normal ( $p < 0.05-0.001$ ) and independent of sex.

More pronounced changes in KI and ILES in the A2 group were higher than normal by 1.8 and 3.8 times, respectively, in women more than in men by 1.7 and 2.1 times ( $p < 0.05-0.001$ ), respectively. ILG was not different from the norm, but was greater in men by 1.2 times ( $p < 0.05-0.001$ ).

In the A3 group, KI and ILES significantly exceeded the norm – 2.1 and 5.1 times ( $p < 0.05-0.001$ ), respectively. Gender dependence on ILES, where the rates for women are 1.7 times higher compared with men. ILG was less than 1.2-fold and non-sex-dependent ( $p < 0.05-0.001$ ). Analyzing changes in KI, ILG, ILES depending on the group of patients A1, A2, A3, it is found out: KI is increased in all patients, and has slight deviations in the groups; ILG in A1

**Table I.** Changes integrative indicators of endogenic intoxication in hiv-infected.

Index	comparison	Group, n								
		A1, n=46			A2, n=11			A3, n=35		
		all	men	women	all	men	women	all	men	women
1	2	3	4	5	6	7	8	9	10	11
Index endogenic intoxication										
LII	0,70± 0,07	1.44±0.2 a	1.35±0.19 a	1.72±0.5 a	1.43±0.35 a	1.25±0.26 a	1.9±0.55 a	1.44±0.22 a	1.38±0.21 a	1.66±0.41 a
ISL	1,62± 0,10	2.77±0.3 a	2.6±0.28 a	3.3±0.8 a	2.71±0.53 a	2.34±0.34 a	3.65±1.0 a	2.79±0.34 a	2.68±0.33 a	3.17±0.72 a
HII	0,64± 0,06	3.15±0.6 a	2.45±0.45 a	5.37±1.96 a	2.87±0.98 a	2.1±0.72 a	5.14±2.1 a	3.2±0.68 a	2.56±0.5 a	5.46±2.09 a
IIS	0,16± 0,02	3.12±0.74 a	2.46±0.58 a	5.24±2.46 a	4.01±1.9 a	2.72±1.2 a	7.44±3.3 a	2.85±0.74 a	2.38±0.57 a	4.41±2.1 a
NRR	12,75± 1,82	32.08±4.49 a, c	30.37±4.93 a, c	37.53±10.6 a	18.63±2.2 a, b	12.47±1.58 a, b	35.05±10.9 a	36.31±5.23 a, c	35.68±5.9 a, c	38.46±9.03 a
Index non-specific reactivity										
IR	4,65± 0,36	3.98±0.39 a	3.98±0.4 a, c	3.96±0.68 a	5.23±0.8 a	5.74±0.4 a, b	3.89±0.42 a	3.58±0.39 a	3.46±0.43 a, c	3.98±0.63 a
NLR	8,88± 0,91	10.86±1.51 a	9.39±0.58 a	15.53±1.43 a	11.34±0.82 a	11.01±0.74 a	12.24±1.24 a	10.71±1.75 a	8.92±0.46 a, c	16.76±3.8 a
LMR	4,77± 0,45	3.64±0.27 a	3.65±0.32 a, c	3.62±0.34 a	4.73±0.6 a	5.15±0.67 a, b	3.61±0.42 a	3.3±0.41 a	3.21±0.42 a, c	3.62±0.35 a
llymph	0,59± 0,04	0.43±0.03 a	0.43±0.05 a	0.44±0.06 a	0.51±0.09 a	0.54±0.097 a	0.42±0.06 a	0.41±0.05 a	0.4±0.05 a	0.44±0.06 a
ELR	0,08± 0,009	0.1±0.004 a	0.09±0.006 a	0.11±0.01 a	0.1±0.004 a	0.1±0.008 a	0.09±0.01 a	0.1±0.004 a	0.09±0.007 a	0.11±0.01 a
Continuation of table I										
1	2	3	4	5	6	7	8	9	10	11
IA	1,05± 0,07	0.83±0.064 a	0.83±0.08 a	0.84±0.07 a	0.99±0.05 a	1.08±0.11 a	0.77±0.12 a	0.78±0.08 a, c	0.75±0.08 a, c	0.87±0.05 a
NI	0,06± 0,01	0.21±0.04 a, c	0.21±0.04 a, c	0.21±0.05 a, c	0.09±0.01 a, b	0.09±0.01 a, b	0.1±0.012 a, b	0.25±0.04 a, c	0.24±0.06 a, c	0.25±0.06 a, c
Index inflammation activity										
KI	2,02± 0,94	4.13±0.26 a	3.84±0.46 a	5.07±1.1 a	3.67±0.38 a	3.05±0.28 a	5.35±1.3 a	4.28±0.63 a	4.08±0.42 a, c	4.96±1.1 a
ILG	4,85± 0,29	4.1±0.24 a	4.14±0.2 a	4.0±0.3 a	4.75±0.33 a	5.01±0.58 a	4.05±0.27 a	3.9±0.37 a	3.88±0.38 a	3.98±0.32 a
ILESR	1,33± 0,20	6.46±0.7 a	5.42±0.75 a	9.77±1.22 a	5.09±1.15 a	3.87±1.14 a	8.37±1.67 a	6.89±0.84 a	5.88±0.9 a	10.3±1.66 a

Annotations. Significant difference in metrics ( $p < 0,05-0,001$ , we used Student's t-criteria): a – about the comparison group; b – about the group A1; c – about the group A2.

and A3 groups is less than normal, unlike patients in A2 group, where it remained within the normal range, but by 1.1 and 1.2 times more that in A1 and A3 ( $p < 0.05-0.001$ ). ILESR in the A1 and A3 groups have similar increased rates, unlike the A2 group, where the index is 1.3 and 1.4 times lower, respectively ( $p < 0.05-0.001$ ).

## DISCUSSION

The obtained changes in patients of group A1 indicate an increase in the level of endogenous intoxication and activation of tissue breakdown processes, marked activity

of the inflammatory process and impaired immunological reactivity. There is a clear systemic response to inflammatory processes in the body of patients, the likely development of decompensated endogenous intoxication [7]. However, the fact that comparing intoxication indices in different sex subgroups, where indicators are higher in women than in men, we can say that the prevalence of pathological phenomena in women.

Comparison of the obtained data indicates the presence of signs of acute inflammatory process [8,9], which is more active in persons of group A2 than in A1, we can also note that signs of acute inflammatory process are more active

in women of group A2. It should be noted that signs of an acute inflammatory process are more pronounced in men from group A2 compared to group A1. There is a pronounced systemic response to inflammatory processes in the body of patients in both groups, and the degree of endogenous intoxication and activation of tissue decay processes in the subjects does not differ. Immune reactivity is impaired, which has a more pronounced development in A2 group women. The development of decompensated endogenous intoxication is less intense in the A2 group and more active in women [10].

The severity of the acute inflammatory process is less intense in people in group A3 than others. The activity of increasing the level of endogenous intoxication and activation of tissue decay processes in the subjects of this group is not different.

Immune reactivity disorders of the same intensity are observed in all groups.

Decompensated endogenous intoxication is more pronounced in HIV-infected A3 groups than in A1 and A2, more pronounced in women.

All HIV-infected people have a shift of the leukocyte formula to the left, activation of a non-specific inflammatory process, development of autoimmune processes, predominance of slow-type reactions over immediate-type hypersensitivity. Also, an inflammatory response of mild severity, changes in white shoots of blood, and antigenic and cytokine stimulation have been established – this testifies to the intoxication of patients and the loss of the ability of neutrophils to eliminate antigens, which is explained by the increase in young forms of rod-shaped neutrophils. The described pathological phenomena are more clearly manifested in women. We observe an active adaptive response of white blood and the immunodeficiency state of the cell type, a decrease in nonspecific anti-infection protection of the examined [11,12]. It can be argued that A2 patients have a tendency to develop a septic condition [13-15], with men at greater risk of developing. People in group A3 were characterized by the development of intoxication, an inflammatory reaction that was more intense in women. Shifting the leukocyte formula to the left, the activation of nonspecific inflammatory processes with the development of autoimmune phenomena have a more active course in women in this group. Patients of this group are characterized by the development of intoxication, an inflammatory reaction of mild severity; development of endogenous intoxication and impaired immunological reactivity due to auto-intoxication of the body in the destruction of own cells under the influence of bacterial toxins [12-15].

## CONCLUSIONS

1. Middle-aged men are predominantly HIV positive. The systemic immune response to acute inflammatory processes is present in all examined patients, more pronounced in women, higher in patients with I, II, and III stages of the disease, which is confirmed by an increase in indicators of LII, ISL, HII, IIS, NRR.
2. In all study groups there is a progressive ( $A1 \leq A2 \leq A3$ ) impaired immunological reactivity, which is accompa-

nied by significant fluctuations and more pronounced in women, towards an increase (ELR, NLR, NI), or a decrease (IA, Ilymph), indicating immunodeficiency cell type with reduction of nonspecific anti-infective protection, shift of leukocyte formula to the left, development of autoimmune processes, predominance of slow-type reactions over immediate-type hypersensitivity, leading to sensitization of the body, triggering of allergic mechanisms of background intoxication.

3. In patients with stage IV HIV infection, there are processes of moderate and severe inflammatory reactions, impaired reactivity due to auto-intoxication of the body in the destruction of own cells under the influence of bacterial toxins, more pronounced in women, which is confirmed by an increase of KI and ILESR with decreasing ILG.

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#### **Conflict of interest:**

*The Authors declare no conflict of interest*

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**A** – Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article