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BLOOD INTEGRATED INDICATOR OF OXIDATIVE STRESS IN INFANTS BORN TO HIV-INFECTED MOTHERS

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A single-center cross-sectional study was conducted from March 2020 to January 2021 and included 142 neonates born with a gestational age of more than 37 0/7 weeks. The aim of the work was an individual assessment of the oxidative stress index (OSI) in newborns of HIV-infected mothers. Materials and methods: the state of the LPO–AOD system was assessed by determining the content of lipid peroxidation oxidation substrates with conjugated double bonds (DB), diene conjugates (DC), ketodienes and conjugated trienes (KD and CT), TBA-active products in the blood (TBA-AP), retinol, α-tocopherol, reduced (GSH) and oxidized glutathione (GSSG), superoxide dismutase (SOD) activity. OSI was used to evaluate differences in lipid peroxidation processes in HIV-exposed uninfected newborns. Results: The index of oxidative stress in the group of HIV-exposed uninfected newborns was detected 1.98 times higher compared to healthy newborns and was 2.5 and 1.26, respectively. The value of the oxidative stress coefficient indicates a significant imbalance in the LPO-AOP system reflecting the enhancement of the lipid peroxidation processes. An increase in the concentration of substrates and products of peroxidation leads to the destruction of lipids, and, consequently, to the degradation of the cell membrane complex. Conclusion: The integral oxidative stress index is recommended as a general indicator that characterizes the level of lipid peroxidation products and antioxidant protection factors in a particular group. Also, OSI is more sensitive indicator than separated components of the system, which objectively represents the LPO–AOD system malfunctioning, and provides the comprehensive view to the both lipid peroxidation processes and the level (effectiveness) of protective factors. To summarize, the results of the study point to the need to further investigations aimed to determination of prognostically significant markers in PVEN, which could be involved or could indicate the pathological processes both in the early neonatal period and in the later stages of infant development.

Keywords: newborns, HIV-infected pregnant women, HIV infection, oxidative stress, integral index.

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Oxidative stress (OS), resulting from increased free radical processes and a decrease in the buffer capacity of antioxidant defense (AOD), is one of the main factors in the pathogenesis of many diseases [1, 2, 3, 4, 5, 6]. In clinical practice, both in the analysis of pathological conditions and in the detection of disorders caused by environmental factors, integral indicators are used, since they are more sensitive in assessing the balance of LPO–AOD processes than comparing separate markers [3, 4, 5]. This is due to the fact that the complexity and multicomponent nature of the LPO–AOD system makes it difficult to quantify oxidative stress and, accordingly, interpret the results. The methodology for individual assessment of the Oxidative stress index (OSI) as a single systemic indicator for characterizing disorders in the LPO–AOD system is one of the most relevant today.

On the one hand, over the past decades there has been observed a significant decrease in mother-to-child HIV-transmission frequency to 1.5%. [7, 8]. On the other hand, advanced methods of providing medical care to HIV-positive pregnant women and modified approaches for prescribing antiretroviral therapy (ART) have significantly increased the number of perinatally HIV-exposed uninfected infants [9]. Underestimation of the clinical status and risks specific to this cohort of children leads to an increase in adverse neonatal outcomes. Perinatally HIV-exposed uninfected children have a higher incidence of morbidity and mortality, an increased risk of a complicated course of infectious diseases, immunological disorders and disorders of neuropsychic development [14]. It is assumed that unfavorable outcomes are associated with the direct and indirect effects of HIV, exposure to ART and with comorbidity [10]. A large number of studies have been devoted to the study of immunological disorders in perinatally HIV-exposed uninfected children. It has been shown that at birth there is impairment of the activation and differentiation of T- and B-cells and increase in some markers of inflammation and activation of monocytes, which persist up to 6 months of life and are not associated with the inflammatory status of the mother. It is also suggested that oxidative stress may be a potential cause of long-term persistence of inflammatory markers in perinatally HIV-exposed uninfected children. In addition, maternal ART can cause fetal mitochondrial toxicity, which in turn leads to the development of oxidative stress. It has also been shown that the effects of mitochondrial toxicity in a child can persist for a year after intrauterine exposure

to antiretroviral drugs [11, 12, 13]. At the same time, the monitoring integrative indicators of oxidative stress in perinatally HIV-exposed uninfected children remains relevant to determine prognostically significant factors in the development of pathological processes both in the early neonatal period and at later stages of child ontogenesis.

The aim of this work was an individual assessment of OSI in newborns of HIV-infected mothers.

Materials and methods. A single-center cross-sectional study was conducted from March 2020 to January 2021 and included 142 neonates born in the Irkutsk City Perinatal Center with a gestational age of more than 37 0/7 weeks.

All newborns were divided into 2 groups: the main group included 62 children from HIV-seropositive mothers, the control group consisted of 80 full-term newborns from HIV-seronegative mothers.

Criteria for inclusion in the main group: infants born alive at a gestational age of more than 37 0/7 weeks; confirmed HIV infection in mothers; informed consent signed by parents and / or legal representatives. *Criteria for exclusion from the main group:* parents and/or legal representatives refuse to take part in the study at any stage; a newborn from a discordant couple; a child with hemolytic disease of the newborn; a child with chromosomal diseases; infants born to PCR-confirmed SARS-CoV-2 positive mothers or confirmed mother`s vaccination against COVID-19 in the third trimester of pregnancy; the patient does not meet the inclusion criteria.

Depending on the HIV viral load in HIV-infected mothers before childbirth (at a gestational age of 34 weeks or more), newborns of the main group were divided into two subgroups: in the 1st subgroup of children (n=41), the HIV viral load in their mothers had a detectable value (more than 50 copies/ml), in the 2nd subgroup of children (n=21) the mothers` HIV viral load was undetectable (less than 50 copies/ml).

Criteria for inclusion in the control group: newborns born alive at a gestational age of more than 37 0/7 weeks; HIV-negative mothers, informed consent signed by parents and / or legal representatives of the child. *Criteria for exclusion from the control group:* children with hemolytic disease of the newborn, chromosomal diseases; infants born to PCR-confirmed SARS-CoV-2 positive mothers or confirmed mother`s vaccination against COVID-19 in the third trimester of pregnancy; the patient does not meet the inclusion criteria. The groups of newborns were comparable on gestational age, anthropometric parameters at birth and Apgar score ($p > 0.05$).

The study was conducted in accordance with the principles of the WMA Declaration of Helsinki (2013 edition); the experiment was approved by the Biomedical ethics committee at the Federal state public scientific institution «Scientific center for family health and human reproduction problems» (extract from the Minutes of the meeting No. 2 dated 04.03.2021). Informed consent for the inclusion in the study was signed by the parents and/or legal representatives of the child.

All mothers of newborns of the main group were prescribed antiretroviral therapy (ART) by the infectiologist of the regional AIDS Center to prevent the transmission of HIV infection from mother to child during pregnancy (the first stage of PMTCT). The particular type of ART regimen was prescribed considering its effectiveness, dynamics of the viral load (VL) and the absence of contraindications. Prevention of transmission of HIV infection during childbirth (intravenous administration of zidovudine) was performed in all mothers of newborns of the main group (second stage of PMTCT) (Clinical guidelines "HIV infection in pregnant women", 2021). The need of prophylactic ART scheme in newborns of the main group depended on the risk of HIV transmission from mother to child (the third stage of PMTCT). Children were prescribed zidovudine monotherapy for a period of 4 weeks in case of undetectable HIV-VL in mother before delivery (at a gestational age of 34 weeks or more). At mother`s HIV-VL level of more than 50 copies/ml the risk of HIV transmission was considered high and newborns of the main group were prescribed three-component ART for a period of 4 weeks (zidovudine, lamivudine and nevirapine) (Clinical guidelines "HIV infection in children", 2020).

All children of the main group were HIV-negative according to PCR testing. After birth all newborns of the main group were formula fed to prevent HIV infection. Children from the control group were breastfed.

Blood plasma and erythrocyte hemolysate were used as biological samples. Blood was collected on the 3rd day of life in the morning before feeding from a peripheral vein (back of the hand) using disposable vacuum systems with a 23G needle into tubes with EDTA-K3. All children underwent analgesia (non-pharmacological methods of pain correction - non-nutritive sucking and 20% glucose solution per os).

To assess the intensity of lipid peroxidation processes, the concentrations of the substrates with double bonds (DB) and oxidation products: diene conjugates (DC), ketodienes, conjugated trienes (KD and CT), active products of thiobarbituric acid (TBA-AP) were measured. The activity of the components of the antioxidant defense system was assessed by the value of total antioxidant activity of blood serum (AOA), based on the concentrations of natural endogenous antioxidants (α-tocopherol and retinol) oxidized (GSSG), reduced (GSH) glutathione and superoxide dismutase (SOD) activity. The measurements were carried out using spectrophotometric and fluorometric methods.

The acknowledged method of calculating the oxidative stress index (OSI) was used in order to individual assessment of oxidative stress and was based on the ratio of pro- and antioxidant factors [8].

$$OSI = ((ДСi/ДСn) \times (TBA\text{-}AP\ i)/(TBA\text{-}AP\ n) \times (KD\_CTi/KD\_CTn)) / ((SODi/SODn) \times (\alpha\text{-}TOCOFEROLi/\alpha\text{-}TOCOFEROLn) \times (RETINOLi/RETINOLn) \times (GSHi/GSHn)),$$

note: «i» – the levels of indicators of the examined patients; «n» - levels of indicators of the control group.

Normally, the oxidative stress index tends to 1 [8]. The value of OSI > 1 is considered as an increase in the degree of oxidative stress. The greater the value of the oxidative stress index, the more intense the processes of lipid peroxidation and the less effective the AOD system.

The data was processed using the Statistica 6.10 software (StatSoft, Inc.). The visual-graphic method and Kolmogorov-Smirnov`s criterion with Lilliefors and Shapiro-Wilk`s corrections were used to determine the proximity to the normal law of distribution. The equality of general variances was tested with Fisher's F-test. The nonparametric Mann-Whitney test was used to compare the main and control groups. Differences were considered significant at $p<0.05$.

Results and discussion. Since there were no significant differences between groups of newborns when comparing the indicators of the "LPO-AOD" system, depending on the mothers` HIV viral load in, the newborns were combined into one group. Also, the groups of newborns were comparable on maturity and Apgar score. Intergroup differences during the period of early postpartum adaptation and early neonatal period were not found in the compared groups. At the time of delivery and the course of pregnancy, the

mothers of the control group and the HIV group were comparable and did not have statistically significant differences.

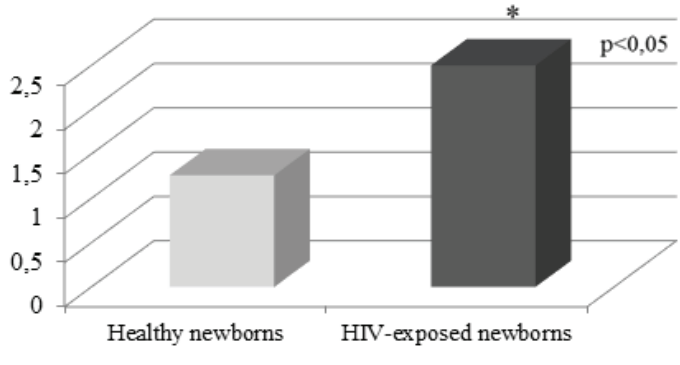
In the blood of HIV-exposed uninfected newborns, a statistically significant increase in substrates with double bonds (DB), the level of primary (DC) and final products (TBA-AP) of lipid peroxidation were found. The antioxidant defense system was characterized by decrease in the levels of total blood AOA, SOD and α-tocopherol with increased retinol concentration (Table). The index of oxidative stress in the group of HIV-exposed uninfected newborns was detected 1.98 times higher compared to healthy newborns and was 2.5 and 1.26, respectively (Figure).

cal in various pathological conditions, the mechanisms of their development may have specific features. Accumulation of free radical oxidation products in chronic diseases causes damage of the vascular endothelium with subsequent development of the endothelial dysfunction [3, 5]. In acute inflammation the development of oxidative stress is characterized by the rate of accumulation and an excessive increase in the concentration of metabolites, when the body does not have time to mobilize its own antioxidant reserve, which contributes to the aggravation of free radical oxidation reactions and hyperactivation of the immune system [2, 4].

The integral oxidative stress index is recommended as a general indicator that

Parameters of the LPO-AOD system in healthy and HIV-exposed newborns

Index	Healthy newborns. n=80	HIV-exposed uninfected newborns. n=62
DB. units	1.96 (1.39; 2.47)	2.12 (1.94; 2.62)
KD и CT. units	0.56 (0.42; 0.79)	0.76 (0.53; 0.98)
DC μmol/l	1.09 (0.72; 1.44)	1.33 (1.16; 1.68)
TBK-AP. μmol/l	1.07 (0.71; 1.52)	1.35 (1.13; 1.74)
AOA. units	1.52 (1.29; 1.75)	1.29 (1.15; 1.57)
retinol. μmol/l	0.49 (0.36; 0.6)	0.61 (0.46; 0.69)
α-tocopherol. μmol/l	9.29 (7.33; 11.26)	7.58 (6.53; 9.42)
GSH. mmol/l	2.22 (1.94; 2.41)	2.15 (1.74; 2.61)
GSSG. mmol/l	1.95 (1.62; 2.19)	1.85 (1.54; 2.14)
SOD. units	1.47 (1.39; 1.52)	1.42 (1.33; 1.52)



Oxidative stress index in groups of healthy and HIV-exposed newborns

The value of the oxidative stress coefficient indicates a significant imbalance in the LPO-AOP system reflecting the enhancement of the lipid peroxidation processes. An increase in the concentration of substrates and products of peroxidation leads to the destruction of lipids, and, consequently, to the degradation of the cell membrane complex. Despite the fact that free radical processes are typi-

characterizes the level of lipid peroxidation products and antioxidant protection factors in a particular group. Also, OSI is more sensitive indicator than separated components of the system, which objectively represents the LPO–AOD system malfunctioning, and provides the comprehensive view to the both lipid peroxidation processes and the level (effectiveness) of protective factors.

To summarize, the results of the study point to the need to further investigations aimed to determination of prognostically significant markers in PVEN, which could be involved or could indicate the pathological processes both in the early neonatal period and in the later stages of infant development. In order to improve the medical care of PVEN, it is necessary to continue research and develop clinical recommendations for managing this category of newborns at all stages of nursing and treatment.

Reference

1. Kurashova N.A., Vanyarkina A.S., Petrova A.G. [et al.] Features of the free radical oxidation process and antioxidant system in newborns born to HIV-infected of mothers who received antiretroviral therapies to prevent HIV transmission. Bulletin of Experimental Biology and Medicine. 2023; 174(4): 413-416 (In Russ.).] doi: 10.1007/s10517-023-05719-z

2. Kolesnikova L.I., Kolesnikov S.I., Darenskaya M.A. [et al.]. Ocenka pro- i antioksidantnogo statusa u zhenshchin s VICH i koinfekciej [Evaluation of the pro- and antioxidant status of women with HIV or coinfection]. Terapevticheskij arhiv [Therapeutic archive. 2016; 88(11): 17-21 (In Russ.).] doi: 10.17116/terarkh2016881117-21

3. Kolesnikova L.I., Madaeva I.M., Semenova N.V. [et al.]. Ocenka okislitel'nogo stressa u zhenshchin s narusheniyami sna v postmenopauze s ispol'zovaniem integral'nogo pokazatelya [The evaluation of oxidative stress in women with sleep disturbances in post menopause conditions using integrated indicator]. Klinicheskaya laboratornaya diagnostika [Clinical laboratory diagnostics. 2014; 59(12): 29-32 (In Russ.).]

4. Kolesnikova L.I., Grebenkina L.A., Kurashova N.A. [et al.]. Ocenka processov perekisnogo okisleniya lipidov i antioksidantnoj zashchity u muzhchin s hronicheskoj monotrihomonadnoj infekciej s pomoshch'yu koefficienta okislitel'nogo stressa [Evaluation of processes of lipid peroxidation and antioxidant protection in men with chronic monotrichomonas infection by the factor of oxidative stress]. Byulleten' Vostochno-Sibirskogo nauchnogo centra Sibirskogo otdeleniya Rossijskoj akademii medicinskih nauk [Bulletin of East Siberian Scientific center SB RAMS. 2011; 77(1): 74-76 (In Russ.).].

5. Kolesnikova L.I., Kurashova N.A., Dolgih M.I. [et al.]. Primenenie integral'nogo pokazatelya dlya ocenki okislitel'nogo stressa u muzhchin s patospermiej i saharnym diabetom 1 tipa [Application of integral indicator for assessment of oxidative stress in men with pathospermia and type 1 diabetes]. Urologiya [Urology. 2015; 4: 71-75 (In Russ.).]

6. Leshchenko O.Ya., Genich E.V. [et al.]. VICH i fertil'nost': nejroendokrinnye i metabolicheskie aspekty [HIV and infertility: neuro-endocrine and metabolic aspects]. VICH-infekciya i immunosupressii [HIV infection and immunosuppression. 2020;12(4): 73-80 (In Russ.).] doi: 10.22328/2077-9828-2020-12-4-73-80

7. Kurashova N.A., Vanyarkina A.S., Petrova A.G. [et al.]. Dlina telomer lejkocitov u novorozhdyonnyh ot VICH-inficirovannyh materej [Length of leukocyte telomeres in newborn from HIV-infected mothers]. Byulleten' eksperimental'noj biologii i mediciny [Byulleten' eksperimental'noj biologii i mediciny. 2023; 175(2): 227-232 (In

Russ.).] doi: 10.47056/0365-9615-2023-175-2-227-232.
8. Rashidova M.A., Sholokhov L.F., Marianian A.Yu. [et al.]. VICH i beremennost': realii XXI veka [HIV and pregnancy: realities of XXI century]. Sibirskij nauchnyj medicinskij zhurnal [Sibirskij nauchnyj medicinskij zhurnal. 2022; 42(2): 10-17. (In Russ.).] doi 10.18699/SSMJ20220202.
9. Voronin E.E., Latysheva I.B. Voronin E. E., Latysheva I.B. VICH-infekciya u beremennyh zhenshchin i detej v Rossijskoj Federacii [HIV infection in pregnant women and children in the Russian Federation]. Materialy konferencii «Aktual'nye voprosy VICH-infekcii. Ohrana zdorov'ya materi i rebyonka» [Materials of the conference "Topical issues of HIV infection. Maternal and child health." SPb.: Man and his health; 2022: 3–5 (In Russ.).]
10. Sevenoaks T, Wedderburn CJ, Donald KA. [et al.]. Association of maternal and infant inflammation with neurodevelopment in HIV-exposed uninfected children in a South African birth cohort. Brain Behav Immun. 2021; 91:65-73. doi: 10.1016/j.bbi.2020.08.021.
11. Dirajlal-Fargo S, Mussi-Pinhata MM, Weinberg A. [et al.]. NISDI LILAC Protocol. HIV-exposed-uninfected infants have increased inflammation and monocyte activation. AIDS. 2019; 33(5): 845-853. doi: 10.1097/QAD.0000000000002128.
12. Ross AC, Leong T, Avery A. [et al.]. Effects of in utero antiretroviral exposure on mitochondrial DNA levels, mitochondrial function and oxidative stress. HIV Med. 2012; 13: 98–106.
13. Zidar DA, Juchnowski S, Ferrari B. [et al.]. Oxidized LDL Levels Are Increased in HIV Infection and May Drive Monocyte Activation. J Acquir Immune Defic Syndr. 2015; 69: 154–160.
14. Prendergast AJ, Evans C. Children who are HIV-exposed and uninfected: evidence for action. AIDS. 2023; 37(2): 205-215. doi: 10.1097/QAD.0000000000003409.

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ANALYSIS OF THE C.757A>G P.(ILE253VAL) VARIANT OF THE *SLC26A4* GENE IN *GJB2*-NEGATIVE PATIENTS WITH HEARING LOSS IN YAKUTIA

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In this work, we searched for the missense variant c.757A>G p.(Ile253Val) of the *SLC26A4* gene in *GJB2*-negative patients with hearing loss (n=201) and in the control group of hearing individuals (n=103) in Yakutia. As a result, this variant was detected with a frequency of 2.02% among patients, in the control group - 1.94%. To interpretation the clinical significance, a frequency analysis of this variant and *in silico* evaluation were performed, the results of which are in favor of the likely benign of the c.757A>G p.(Ile253Val) variant of the *SLC26A4* gene, as indicated by the high frequency of occurrence in population samples, and the fact that this missense substitution theoretically does not violate the structural stability of the pendrin protein (SLC26A4).

Keywords: variant c.757A>G p.(Ile253Val), *SLC26A4* gene, pendrin (SLC26A4), sensorineural hearing loss.

Introduction. Hearing impairment (HI) is one of the most common congenital pathologies. The prevalence of congenital and childhood hearing loss (HL) and deafness in the world is estimated at 1.33 per 1000 newborns [19]. It is known that up to 50% of cases of congenital deafness have a hereditary etiology [6, 19]. About 70% of genetic causes of HL are thought to be nonsyndromic, with the remaining 30% being syndromic. At the same time, approximately 75% of all cases of nonsyndromic HL and deafness occur in autosomal recessive forms [6, 19].

The contribution of the *SLC26A4* gene to the etiology of autosomal recessive forms of HL is considered one of the most significant, and the proportion of its pathogenic variants among all identified causative variants of other genes in a number of regions of the world is in second place after the *GJB2* gene [5, 7, 9, 10, 16, 31], and in some and in first place (Pakistan) [12]. Pathogenic variants of the *SLC26A4* gene are associated with both autosomal recessive deafness type 4 (DFNB4, OMIM #600791) and Pendred syndrome (PS, OMIM #274600). The *SLC26A4* gene is located on chromosome 7 at the locus 7q22–q31, contains 21 exons, and encodes a transmembrane protein known as pendrin (PDS), which is expressed in the inner ear, thyroid gland, kidneys and airway epithelium [21-24, 28, 30]. Pendrin consists of 780 amino acids forming 12–14 TM segments, including a segment of the intracellular functional STAS domain (Sulfate Transporter and Anti-Sigma factor antagonist) [15, 29].

Earlier in Yakutia, using direct Sanger sequencing of the coding region of the *SLC26A4* gene, an analysis of its mutational contribution was carried out among six patients with HI and inner ear anomalies (IP-1, IP-2, and EVA) [1]. Five variants were identified in the *SLC26A4* gene: c.85G>C p.(Glu29Gln), c.757A>G p.(Ile253Val), c.2027T>A p.(Leu676Gln), c.2089+1G>A (IVS18 +1G>A) and c.441G>A p.(Met147Ile). Pathogenic biallelic variants of the *SLC26A4* gene were detected in four patients (4/6) and monoallelic *SLC26A4*-variants of in two patients (2/6). It should be noted that all monoallelic patients were Yakuts and carried the same heterozygous variant of the *SLC26A4* gene - c.757A>G p.(Ile253Val) [1]. In the ClinVar database, this variant is not annotated (https://www.ncbi.nlm.nih.gov/snp/rs773657545/#publications). However, in the Deafness variation database (DVD), the c.757A>G p.(Ile253Val) variant is classified as likely pathogenic

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