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Research article

ASSESSING RISKS OF HEPATOBILIARY DISORDERS IN CHILDREN UNDER COMBINED EXPOSURE TO PERSISTING HERPES AND TECHNOGENIC CHEMICALS

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Chronic persistent viral infection leads to developing immune deficiency and may induce lesions in many organs, the hepatobiliary system included. This, in its turn, may facilitate the onset of diseases of the digestive system under exposure to technogenic chemicals, especially those able to produce hepatotoxic effects.

In this study, our aim was to examine risks of developing hepatobiliary disorders in children under combined exposure to persisting herpes infection and technogenic chemicals.

We conducted a clinical examination of 324 children aged between 6 and 17 years living either in a large industrial city or on a territory where the sanitary-hygienic situation was favorable. The examination included a clinical checkup, laboratory diagnostic tests identifying herpes markers, chemical analyses aimed at establishing levels of technogenic chemicals in blood, and ultrasound scanning of hepatobiliary organs.

We established that exposure to airborne technogenic chemicals created elevated levels of aromatic hydrocarbons and formaldehyde in 64.9–97.6 % of the exposed children; elevated manganese and chromium levels, in 20.8–34.6 % of them. Markers of cytomegalovirus (CMV) and Epstein Barr virus (EBV) were detected in 75 % of the exposed children; each second child had HSV-1 or HSV-2; each third child had human herpesvirus 6. Hepatobiliary disorders occurring under combined exposure to persistent herpes and technogenic chemicals were represented by structural liver changes in 30.8 % of the examined children; abnormally shaped gallbladder or reactive changes in its walls and dyscholia, in 15.7–48.8 %;. These disorders entail elevated levels of direct bilirubin and greater ALT against imbalance of oxidant and antioxidant systems and manifest themselves as biliary pathology in 69.5 % of cases. Exposed children with persistent herpes infection have 1.2–2.3 times higher likelihood of developing structural changes in the liver and gallbladder pathology and up to 4.3 times higher risks of biliary dysfunction and chronic gastroduodenitis.

Keywords: *children, hepatobiliary disorders, relative risk, persistent herpes, technogenic chemicals, HSV (herpes simplex virus), cytomegalovirus, Epstein Barr virus, hepatotoxicity.*

At present, prevalence of gastrointestinal disorders among children remains high, both in Russia and worldwide [1–7]. Functional disorders of the gastrointestinal tract usually occur in preschoolers and tend to have continuous recurrent clinical course. In adolescence, this may lead to chronic gastroduodenal and hepatobiliary pathology, which, in its turn, results in much poorer quality of life for children and adolescents [1, 8–11].

Nowadays, well-developed transport infrastructure and growing production volumes create substantial chemical pollution of the environment [12, 13]. According to the WHO, ambient (outdoor) air pollution is the second significant factor able to cause non-communicable diseases

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[14]. Multiple epidemiological studies report that population morbidity, that of gastrointestinal disorders included, tends to be higher in RF regions with highly developed industry [15–17].

Anthropogenic environmental pollutants are mostly introduced into the body orally and / or by inhalation. They are removed from the body by detoxification that takes place predominantly in the liver. Damage to the latter can be associated not only with hepatotoxic effects of xenobiotics but also products of their biotransformation [15, 16, 18, 19]. Technogenic chemicals, apart from their ability to affect target organs directly, can also disrupt the endocrine regulation, induce depletion of energy and plastic resources of various organs and systems in the body and, consequently, facilitate development of various pathologies [19–21].

At present, herpes infection is widely spread among all population groups due to its persistence and long-term symptomless circulation of herpes viruses in the human body starting from childhood [22–25]. Herpes viruses are known to be able to induce functional immunodeficiency thereby facilitating chronic inflammation; they are also able to affect lymphoid tissue cells and liver cells inducing dystrophic changes of hepatocytes and cholestasis in the latter [24–29].

According to some researchers, infectious epidemic processes are changing under the contemporary conditions. Infectious pathologies have been shown to be more prevalent on territories with high levels of technogenic environmental pollution and they tend to be chronic there more frequently [30, 31]. However, little attention has been paid to examining peculiarities of herpes infection under exposure to anthropogenic environmental factors.

Therefore, it seems relevant to examine how hepatobiliary disorders develop in children with herpes infection under exposure to airborne technogenic chemicals.

The aim of this study was to examine risks of developing hepatobiliary disorders in children under combined exposure to persistent herpes infection and technogenic chemicals.

Materials and methods. To examine peculiarities of hepatobiliary disorders, we performed clinical examination of 213 children who were selected by random sampling (46.9 % boys and 53.1 % girls, the mean age being 9.84 ± 0.21 years). The children lived on a territory with developed industry in the Perm Krai where ambient air was polluted with aromatic hydrocarbons (benzene and xylenes), average daily levels of formaldehyde were 1.7 times higher and average manganese levels were 4.8 times higher than the established reference levels under chronic inhalation exposure (RfC_{chr}) ($p < 0.05$); average daily chromium levels were 2.6 times higher than on the reference territory ($p < 0.05$). The reference group was made of 111 children (54.1 % boys and 45.9 % girls, the mean age being 9.49 ± 0.29 years) living on a territory where the sanitary situation was relatively favorable. Both groups were comparable in terms of social indicators and sex ($p = 0.219–0.339$). An acute respiratory infection, any exacerbation of a chronic somatic pathology or an organic pathology of the nervous system detected during the clinical examination was used as an exclusion criterion.

The performed clinical examination conformed to the ethical principles stated in the Declaration of Helsinki (with 2008 alterations and addenda) and the RF National Standard GOST R 52379-2005 Good Clinical Practice (ICH E6 GCP)[1]. It was approved by the Ethics Committee of the Federal Scientific Center for Medical and Preventive Health Risk Management Technologies (The Meeting Report no. 8, 2021). Prior to the study, legal representatives of the examined children gave their informed voluntary consent to medical interventions.

The clinical examination of the children included medical and social questioning, checkups by a pediatrician and gastroenterologist, analysis of child's medical records (the Form no. 112/u and no. 026/y-2000), laboratory diag-

[1] GOST R 52379-2005. Good Clinical Practice (GCP): the RF National Standard; approved by the Order of the Federal Agency on Technical Regulation and Metrology on September 27, 2005 no. 232-st. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/1200041147 (June 10, 2023) (in Russian).

nostics (complete blood count, biochemical blood tests, ELISA tests to identify IgG titers to herpes simplex virus 1 and 2 (HSV1,2), cytomegalovirus (CMV), NA-antigens of Epstein – Barr virus (EBV-NA), PCR of buccal epithelium swabs to identify DNA of human herpesvirus 6 (HHV6), cytomegalovirus (CMV), and Epstein – Barr virus (EBV)) and chemical blood analyses. Laboratory diagnostics was accomplished according to conventional procedures; changes in the analyzed indicators were evaluated in comparison with their age-specific physiological norms.

Chemical analyses of technogenic chemicals levels in biological media (blood) were accomplished in accordance with the Methodical Guidelines MUK 4.1.765-99 Quantification of aromatic hydrocarbons (benzene, toluene, ethyl benzene, o-,m-,p-xylene) in biological media (blood) by using gas chromatography, MUK 4.1.2108-06 Determination of phenol mass concentration in biological media (blood) by using gas chromatography, MUK 4.1.2111-06 Identification of mass concentrations of formaldehyde, acetaldehyde, propionaldehyde, butyraldehyde, and acetone in blood samples by using high performance liquid chromatography, MUK 4.1.3230-14 Identification of mass concentrations of chemicals in biological media (blood and urine) by using inductively coupled plasma mass spectrometry[2]. Levels of chemicals in the examined children's biological media were compared with the regional background levels of the same chemicals identified in blood of the children from the reference group who lived on an ecologically clean territory in the Perm Krai.

The study involved evaluating sizes, state and functional peculiarities of hepatobiliary organs. To do that, we performed ultrasound scanning of the liver, gallbladder, extrahepatic biliary tree, and visceral lymph nodes in the abdominal cavity according to conventional procedures on Vividq premium ultrasound system (GE Vingmed Ultrasound AS, Norway) using both convex (1.8–6.0 MHz) and linear transducer (4.0–13.0 MHz). Linear sizes of the examined organs were evaluated as per the standards suggested by I.V. Dvoryakovskiy with colleagues[3].

The obtained data were analyzed using conventional methods of descriptive statistics. We calculated odds ratio (*OR*) and relative risk (*RR*) of hepatobiliary pathology and their 95 % confidence intervals (CI), authenticity of their bottom limit being above 1.0. Cause-effect relations were established by mathematical modeling that relied on univariate dispersion analysis. We used the Fisher's test (*F*), determination co-

[2] MUK 4.1.765-99. Gazokhromatograficheskii metod kolichestvennogo opredeleniya aromaticheskikh uglevodorodov (benzol, toluol, etilbenzol, o-,m-,p-ksilol) v biosredakh (krov') [Quantification of aromatic hydrocarbons (benzene, toluene, ethyl benzene, o-,m-,p-xylene) in biological media (blood) by using gas chromatography]: Methodical Guidelines, approved by G.G. Onishchenko, the RF Chief Sanitary Inspector on July 6, 1999. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/1200039012 (May 06, 2023) (in Russian); MUK 4.1.2108-06. Opredelenie massovoi kontsentratsii fenola v biosredakh (krov') gazokhromatograficheskim metodom [Determination of phenol mass concentration in biological media (blood) by using gas chromatography], approved by G.G. Onishchenko, the Head of the Federal Service for Surveillance over Consumer Rights Protection and Human Wellbeing and the RF Chief Sanitary Inspector on August 9, 2006. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/1200065240 (May 06, 2023) (in Russian); MUK 4.1.2111-06. Izmerenie massovoi kontsentratsii formal'degida, atsetal'degida, propionovogo al'degida, maslyanogo al'degida i atsetona v probakh krovi metodom vysokoeffektivnoi zhidkostnoi khromatografii [Identification of mass concentrations of formaldehyde, acetaldehyde, propionaldehyde, butyraldehyde, and acetone in blood samples by using high performance liquid chromatography], approved by G.G. Onishchenko, the Head of the Federal Service for Surveillance over Consumer Rights Protection and Human Wellbeing and the RF Chief Sanitary Inspector on August 9, 2006. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/1200065243 (May 06, 2023) (in Russian); MUK 4.1.3230-14. Izmerenie massovykh kontsentratsii khimicheskikh elementov v biosredakh (krov', mocha) metodom mass-spektrometrii s induktivno-svyazannoi plazmoi [Identification of mass concentrations of chemicals in biological media (blood and urine) by using inductively coupled plasma mass spectrometry], approved by A.Yu. Popova, the Head of the Federal Service for Surveillance over Consumer Rights Protection and Human Wellbeing and the RF Chief Sanitary Inspector on December 19, 2014. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/495856222 (May 06, 2023) (in Russian).

[3] Ul'trazvukovaya anatomiya zdorovogo rebenka: prakticheskoe rukovodstvo [The ultrasound anatomy of a healthy child: practical guide], the 1st ed. In: I.V. Dvoryakovskii ed. Moscow, Firma-STROM LLC Publ., 2009, 384 p. (in Russian).

efficient (R^2), and the Student's t-test with the statistical significance level taken at $p \leq 0.05$[4].

Results and discussion. The results obtained by chemical analyses of the examined children's biological media revealed aromatic hydrocarbons in their blood ($p < 0.05$). Mean levels of benzene, toluene, and p-, м-xylene were 1.2–4.25 times higher in the children from the test group ($p = 0.013–0.00009$). Two thirds of the children had elevated benzene and p-, m-xylene levels in their blood and elevated toluene levels were detected in 92.1 % of the cases; the same indicators were identified 1.2–1.8 times less frequently in the reference group ($p = 0.004–0.0001$) (Table 1).

Biological media of 19.4–26.3 % of the examined children were contaminated with phenol ($p = 0.157$). Mean formaldehyde levels were statistically significantly higher than the background levels ($p < 0.05$) practically in all the examined children (95.8–97.6 %) and were 1.2 times higher in the test group against the reference one ($p = 0.019$).

Levels of metals were within their background range in the examined children's blood; however, they tended to be 1.2 times higher in the test group against the reference one ($p = 0.033–0.0001$). The children from the test group had elevated manganese levels in blood 2.2 times more frequently than those from the reference group (20.8 % against 9.6 % accordingly, $p = 0.015$); elevated chromium levels were detected in them 1.4 times more frequently (34.6 % against 24.3 %, $p = 0.077$).

Analyses of throat swabs by the polymerase chain reaction revealed human herpesvirus 6 (HHV6) in practically each third examined child; Epstein – Barr virus, in each third examined child; cytomegalovirus, in singleton cases ($p = 0.466–0.804$). The detected viral loads of HHV6, EBV, and CMV DNA did not have any significant differences between the groups ($p = 0.107–0.862$).

Three quarters of the children in the test group and 2/3 of the children in the reference group had IgG antibodies to CMV antigens and EBV-NA ($p = 0.251–0.291$). The number of children with IgG antibodies to HSV1 and HSV2 antigens was 1.2 times higher in the test group ($p = 0.421$) and HSV1 and HSV2 IgG levels were 1.5 times higher in blood serum in the test group against the reference one ($p = 0.00004$) (Table 2).

Table 1

Mean levels of technogenic chemicals in the examined children's blood, mg/dm^3

Chemical	Background level	The test group	The reference group	Validity of intergroup differences (p)
Benzene	0	0.0034 ± 0.00019*	0.0008 ± 0.0001*	0.00009
Toluene	0	0.0023 ± 0.00021*	0.0019 ± 0.00014*	0.0019
O-xylene	0	0.0032 ± 0.0003*	0.0043 ± 0.0005*	0.032
P-, m-xylene	0	0.0036 ± 0.0003*	0.0026 ± 0.0004*	0.013
Phenol	0.0037–0.01	0.0059 ± 0.001	0.0057 ± 0.001	0.703
Formaldehyde	0.005–0.0076	0.041 ± 0.002*	0.033 ± 0.001*	0.019
Manganese	0.009–0.017	0.014 ± 0.0004	0.012 ± 0.0004	0.033
Chromium	0.0007–0.0047	0.0047 ± 0.0003	0.0039 ± 0.0002	0.0001

Note: * means differences from the background level are authentic ($p < 0.05$).

Table 2

Mean levels of IgG antibodies to herpesvirus antigens in blood serum of the examined children, *Me* [25; 75], arbitrary units

Herpesvirus markers	The test group	The reference group	Validity of intergroup differences (p)
HSV1,2 IgG, a.u.	0.68 [0.45; 5.39]	0.45 [0.25; 5.13]	0.00004
CMV IgG, a.u.	2.06 [1.09; 3.00]	2.26 [0.73; 4.37]	0.304
EBV-NA IgG, a.u.	72.21 [16.07; 111.48]	67.74 [0.87; 144.38]	0.771

[4] Chetyrkin E.M. Statisticheskie metody prognozirovaniya [Statistical forecasting procedures]. Moscow, Statistika, 1977, 356 p. (in Russian).

Each second child was established to have markers of several herpesviruses ($p = 0.632$).

The clinical examination revealed gastrointestinal pathology in 84.5–81.1 % of the examined children ($p = 0.436$); within its structure, biliary disorders were identified in 69.5 % of the cases in the test group and this was 1.2 times more frequent than in the reference group (57.7 %, $p = 0.034$). Chronic GIT diseases were 4.3 times more frequent in the test group (15.5 % against 3.6 % in the reference group, $p = 0.001$). Secondary diffuse hepatitis was diagnosed in 17 children from the test group (7.9 % against 3.6 % in the test group, $p = 0.126$). We established an authentic cause-effect relation between developing liver pathology under elevated levels of manganese, chromium, p-m-xylene, toluene, and phenol in blood ($R^2 = 0.127–0.794$; $32.70 \leq F \leq 418.34$; $p = 0.0001$) and HSV1 and HSV2 IgG, CMV IgG, and EBV-NA IgG levels in blood ($R^2 = 0.151–0.709$; $34.66 \leq F \leq 507.29$; $p = 0.0001$). Biliary dysfunction was 1.2 times more likely ($RR = 1.205$; CI: 1.004–1.447) and chronic gastroduodenitis was 4.3 times more likely ($RR = 4.299$; CI: 1.563–11.828) in children under combined exposure to persistent herpesvirus infection and technogenic chemicals.

Dyspeptic symptoms were mentioned 1.5 times more frequently by the children from the test group (83.1 % against 54.5 % in the reference group, $p = 0.0001$); practically half of the children in the test group had stomach pains (54.1 %) and decreased appetite (56.8 %) whereas such symptoms were detected 1.5–3.6 times less frequently in the reference group (14.9 % and 38.6 % of the children accordingly, $p = 0.005–0.0001$). Dyspeptic symptoms in children were established to be 4.1 times more likely under combined exposure to persistent herpesvirus infection and technogenic chemicals ($OR = 4.115$; CI: 2.300–7.361).

Ultrasound scanning of the hepatobiliary organs revealed that 5.7 % of the children in the test group did not have any hepatobiliary pathology and this share was 3.2 times lower than in the reference group ($p = 0.001$) (Table 3). Hepatobiliary disorders in children were established to be 1.15 times more likely under combined exposure to persistent herpesvirus infection and technogenic chemicals ($RR = 1.148$; CI: 1.034–1.275).

Pathological changes in the liver were 1.2 times more frequent in the children from the test group; enlarged liver was identified in 41.3 % of the examined children in both groups. Structural changes in the liver were established to be 1.9 times more frequent in the children from the test group (30.8 % against 16.3 % in the reference group, $p = 0.01$); they were

Table 3

Ultrasound scanning of the liver and gallbladder: the results obtained for two groups of the examined children, %

Indicators	Test group	Reference group	Validity of intergroup differences (p)
Ultrasound scanning did not reveal any deviations from the healthy state of the hepatobiliary organs	5.7	18.5	0.001
Pathological changes in the liver	61.0	51.1	0.121
Enlarged liver	41.3	41.3	1.0
Structural changes in the liver, including:	30.8	16.3	0.01
–reactive	19.2	10.9	0.082
–diffuse	10.5	5.4	0.162
–nidal	1.2	–	–
Pathological changes of the gallbladder, including:	83.7	68.5	0.004
–abnormally shaped gallbladder	48.8	33.7	0.018
–enlarged volume of the gallbladder	45.4	45.7	1.0
–reactive changes of the gallbladder walls	15.7	6.5	0.031
–signs of dyscholia	41.9	30.4	0.066

predominantly reactive (19.2 % of the cases against 10.9 % in the reference group, $p = 0.082$). Likelihood of structural changes in the liver was 2.3 times higher in the test group against the reference one ($OR = 2.286$; CI: 1.204–4.340). We established an authentic cause-effect relation between developing structural changes in the liver under elevated manganese and toluene levels in blood ($R^2 = 0.359–0.743$; $143.55 \le F \le 529.85$; $p = 0.0001$) and HSV1 and HSV2 IgG and CMV IgG levels in blood ($R^2 = 0.743–0.794$; $515.58 \le F \le 780.66$; $p = 0.0001$).

Gallbladder pathologies were 1.2 times more frequent in the children from the test group ($p = 0.004$) (Table 3). Each second child had abnormally shaped gallbladder (the gallbladder bend or contracted gallbladder) and 41.9 % of the children had inadequate viscosity of bile with some sediment (dyscholia); this was detected 1.4 times more frequently than in the reference group (33.7 % and 30.4 % accordingly, $p = 0.018–0.066$). In addition, 15.7 % of the exposed children with persistent herpesvirus infection had some reactive changes of the gallbladder walls (the share was only 6.5 % in the reference group, $p = 0.031$). Likelihood of the gallbladder pathology in children was established to be 1.2 times higher under combined exposure to persistent herpesvirus infection and technogenic chemicals ($RR = 1.223$; CI: 1.049–1.425). We established an authentic cause-effect relation between abnormally shaped gallbladder and dyscholia under elevated manganese, toluene, and p-, m-xylene levels in blood ($R^2 = 0.278–0.729$; $80.16 \le F \le 525.89$; $p = 0.0001$) and reactive changes of the gallbladder walls and levels of HSV1 and HSV2 IgG and CMV IgG in blood ($R^2 = 0.145–0.609$; $28.27 \le F \le 325.78$; $p = 0.0001$).

Reactive hyperplasia of the lymph nodes in the abdominal cavity was detected 1.2 times more frequently in the reference group (67.4 % against 54.1 % in the test group, $p = 0.037$); reactive changes in the lymph nodes located in the hepatobiliary area were the most frequent (in 41.9 % of the cases in the test group and 56.5 % in the reference group, $p = 0.024$). We established an authentic cause-effect relation between developing hyperplasia of the lymph nodes in the hepatobiliary area and HSV1 and HSV2 IgG level in blood as well as the viral load of HHV6 and EBV DNA ($R^2 = 0.519–0.898$; $181.97 \le F \le 1641.69$; $p = 0.0001$).

Laboratory tests revealed the mean values of basic indicators to be within the physiological ranges in the examined children; still, levels of direct bilirubin and C-reactive protein, as well as ALT activity were authentically higher in the children from the test group ($p = 0.032–0.003$). This may indicate a trend towards developing hepatocellular dysfunction (Table 4). Elevated direct bilirubin levels were 1.5 times more frequent in the test group than in the reference one (15.1 % against 10.0 % accordingly, $p = 0.211$). We established an authentic cause-effect relation between elevated direct bilirubin under elevated levels of manganese and phenol in blood ($R^2 = 0.176–0.295$; $54.59 \le F \le 102.65$; $p = 0.0001$).

Imbalance between the oxidant and antioxidant systems was detected in the children from the both groups. Thus, malonic dialdehyde (MDA) levels in blood plasma were higher than the physiological norm in the children from the test group ($p < 0.05$) but also authentically lower than in the reference group ($p = 0.008$). Elevated MDA levels were detected in 53.0–60.9 % of the examined children ($p = 0.180$). We established a relationship between likelihood of elevated MDA levels in blood and elevated formaldehyde levels in blood ($R^2 = 0.388$; $F = 161.45$; $p = 0.0001$) and elevated EBV-NA IgG in blood ($R^2 = 0.446$; $F = 238.72$; $p = 0.0001$). We also identified a decrease in the total antioxidant activity (AOA) of blood plasma in the examined children against the physiological norm ($p = 0.0001$). Decreased AOA levels were identified in 68.9–75.5 % of the analyzed samples ($p = 0.218$). We established an inverse relationship between a decrease in AOA and elevated manganese ($R^2 = 0.209$; $F = 90.91$; $p = 0.0001$) and HSV1 and HSV2 IgG levels in blood ($R^2 = 0.415$; $F = 168.94$; $p = 0.0001$).

Table 4

Results of the laboratory tests obtained for the examined children, *Me* [25; 75]

Indicator	Physiological range	Test group	Reference group	Validity of inter-group differences (p)
Total protein, g/dm^3	60–80	74.0 [71.0; 77.0]	73.0 [70.0; 75.0]	0.013
Albumins, g/dm^3	35–50	44.0 [42.0; 46.0]	43.0 [41.0; 44.0]	0.039
Total bilirubin, μmol/dm^3	0–18.8	10.0 [8.2; 13.4]	9.5 [7.9; 12.1]	0.333
Direct bilirubin, μmol/dm^3	0–4.3	2.8 [1.9; 3.6]	2.3 [1.7; 3.1]	0.032
AST, U/dm^3	6–37	26.0 [22.0; 30.0]	27.0 [23.0; 31.0]	0.410
ALT, U/dm^3	5–42	15.0 [12.0; 18.0]	13.0 [11.0; 16.0]	0.003
Alkaline phosphatase, U/dm^3	71–645	341.0 [249.0; 475.0]	447.5 [356.0; 564.0]	0.0001
Triglycerides, mmol/dm^3	0.3–1.7	0.7 [0.57; 0.97]	0.79 [0.57; 1.01]	0.316
Total cholesterol, mmol/dm^3	3.11–5.44	4.08 [3.58; 4.53]	4.07 [3.67; 4.64]	0.306
CRP, mg/dm^3	0–12	0.45 [0.03; 12.0]	0.3 [0.01; 0.4]	0.024
Malonic dialdehyde, μmol/cm^3	1.8–2.5	2.6 [2.18; 2.96]*	2.81 [2.34; 3.12]*	0.008
Antioxidant activity of blood plasma, %	36.2–38.6	33.82 [29.1; 37.5]*	32.0 [28.7; 36.2]*	0.142

Note: * means authentic differences from the physiological norms ($p < 0.05$).

Conclusions:

1. Under exposure to airborne technogenic chemicals in levels reaching 4.8 $RfC_{chr.}$, 64.9–97.6 % of the examined children had elevated levels of aromatic hydrocarbons and formaldehyde in blood; elevated manganese and chromium levels were identified in 20.8–34.6 % of the cases.

2. Markers of cytomegalovirus and Epstein – Barr virus were identified in 74.5–77.0 % of the exposed children; markers of herpes simplex virus 1 and 2, in 46.5 %; markers of human herpes virus 6, in 31.3 %.

3. Likelihood of structural changes in the liver and gallbladder pathology was established to be 1.2–2.3 times higher for the exposed children with persistent herpesvirus infection. Hepatobiliary disorders manifested themselves in such children as dyspeptic symptoms (stomach pains and decreased appetites) in 83.1 % of the cases; they included structural changes in the liver, abnormally shaped gallbladder, reactive changes of the gallbladder walls, and dyscholia in 48.8 % of the cases and were accompanied with elevated levels of direct bilirubin and ALT activity against the developing imbalance between the oxidant and antioxidant systems.

4. Relative risk of biliary dysfunctions and chronic pathology equals 1.2–4.3 for children under combined exposure to persistent herpesvirus infection and technogenic chemicals.

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