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Prevalence of tuberculosis among perinatally exposed to HIV and HIV-infected children and predictors of its development

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Abstract

Purpose of the study. To establish risk factors for tuberculosis (TB) in children perinatally exposed to HIV and HIV-infected for the development of corrective measures.

Materials and methods. Outpatient records (form No. 025/y) of 216 children perinatally exposed to HIV and 121 children with HIV infection and their parents (281 individuals) were analyzed. The control group consisted of 100 healthy children. Epidemiological (descriptive, evaluative and analytical) and statistical research methods were used in the study.

Results. The likelihood of contact with a patient with an active form of TB was significantly higher in perinatally exposed to HIV and HIV-infected children compared to children in the control group ($p < 0.001$). The risk of TB in HIV-exposed children was 5.3 times higher in foci where both parents were HIV-infected than in foci formed by discordant couples (RR = 5.3; 95% CI 1.7–21.7). Children in study groups who were not vaccinated with BCG had the highest risk of TB compared to children in the control group (RR = 1.9; 95% CI 1.6–2.2).

Conclusion. Risk factors for TB in children perinatally exposed to HIV are untimely vaccination against TB or its absence and living in the foci where both parents are HIV-infected. The predictors of the development of TB in HIV-infected children are household contacts with TB patient , late diagnosis of HIV infection, and late prescription of highly active antiretroviral therapy after the formation of severe immunosuppression.

Keywords: *children exposed to HIV, tuberculosis, risks, predictors*

Ethics approval. The study was conducted with the informed consent of the patients. The research protocol was approved by the Local Ethics Committee of the Ural State Medical University (Approval No. 9, 18.11.2018).

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Распространённость туберкулеза у детей, перинатально экспонированных ВИЧ и ВИЧ-инфицированных, и предикторы его развития

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Аннотация

Цель исследования — установить факторы риска заболевания туберкулёзом (ТБ) детей, перинатально экспонированных ВИЧ и ВИЧ-инфицированных, для разработки коррекционных мероприятий.

Материалы и методы. Проанализированы амбулаторные карты (форма № 025/у) 216 детей, перинатально экспонированных ВИЧ, и 121 ребенка с ВИЧ-инфекцией и их родителей (281 человек). Контрольную группу составили 100 здоровых детей. В работе использованы эпидемиологический (описательно-оценочный и аналитический) и статистический методы исследования.
Результаты. Вероятность контакта с больным активной формой ТБ у детей, перинатально экспонированных ВИЧ и ВИЧ-инфицированных, была достоверно выше относительно детей контрольной группы (p < 0,001). Риски заболевания ТБ у детей, экспонированных ВИЧ, в очагах, где оба родителя были ВИЧ-инфицированными, в 5,3 раза превышали таковые в очагах, сформированных дискордантными парами (RR = 5,3; 95% ДИ 1,7–21,7). Дети исследуемых групп, не вакцинированные БЦЖ, подвержены наибольшему риску заболевания ТБ по сравнению с детьми контрольной группы (RR = 1,9; 95% ДИ 1,6–2,2).
Заключение. Факторами риска заболевания ТБ у детей, перинатально экспонированных ВИЧ, являются несвоевременная вакцинация против ТБ или ее отсутствие и проживание в очаге, где оба родителя были ВИЧ-инфицированными. Предикторами развития ТБ у ВИЧ-инфицированных детей был контакт с больными ТБ в семье, поздняя диагностика ВИЧ-инфекции и назначение высокоактивной антиретровирусной терапии позже 6 мес после постановки диагноза на фоне сформировавшейся иммуносупрессии.

Ключевые слова: *дети, экспонированные ВИЧ, туберкулез, риски, предикторы*

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Introduction

According to the World Health Organization (WHO), people infected with HIV account for 9% of the number of tuberculosis (TB)[1]cases; people living with HIV are 18 (15–21) times more likely[2] and children are 42 times more likely to develop active TB disease than people without HIV [1].

There are scarce data on the TB incidence among HIV-infected children, and the available information is difficult to interpret due to the problems with diagnosis, under-ascertainment, and selection of study populations. WHO estimates that the HIV prevalence among children with TB ranges from 10 to 60%, and varies depending on the background rates of HIV infection [2].

In 2018, the estimates made by O.B. Nechaeva for TB incidence among HIV-infected population resident in Russia were compared with estimates of TB incidence among the non-infected population. It was found that TB infection was 58.6 times more common among HIV-positive people than among HIV-negative people (1764.3 per 100 thousand HIV-infected people against 30.1 per 100 thousand population without HIV) [3].

The situation was aggravated by the increasing percentage of people with HIV/TB coinfection along with the increasing number of patients with late-stage HIV infection. In 2008–2017, in Russia, the incidence of concomitant infections (HIV and TB) increased by 3.5% (5.2‰ in 2008 against 7.1‰ in 2017) [4]. Higher mortality rates were observed in TB and HIV coinfected patients; in 2018, the mortality reached 23% among the newly diagnosed HIV and tuberculosis patients [5].

With the increasing number of coinfection (HIV + TB) cases among adults, the probability of children being infected increases from 60 to 85% [6, 7]. Multiple studies show that the increased TB incidence among children was caused by children's living in households with HIV-infected adults [8].

TB in HIV-infected children has its specific characteristics: High frequency of disseminated forms (71%) and high mortality, especially among children under 2 years of age due to functional immaturity of their immune system [9, 10].

HIV-infected children with more advanced HIV disease are at higher risk of combination of extrapulmonary and pulmonary TB disease, including its dissemination [11]. The most severe clinical forms of TB, according to most of the authors, develop in patients with the advanced stage of HIV infection in the absence of highly active antiretroviral therapy (HAART) [12].

The group most vulnerable to TB is represented by children under 3 years of age, especially in TB-affected households, due to almost non-existing health technologies and preventive treatment [13].

Multiple studies emphasize the role of social and living conditions in development of TB in any groups of patients; they have an impact on the premorbid back-

[1] UNAIDS. Fact Sheet, Global HIV statistics. URL: https://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_ru.pdf
[2] WHO. Tuberculosis fact sheet, October 14, 2020. URL: https://www.who.int/ru/news-room/fact-sheets/detail/tuberculosis

ground and on the course of the disease [14]. Among the most adverse factors, most of the authors point out alcohol dependence and drug addiction of adult members of the family (at least, of the mother), low incomes and unfavorable ethical and emotional family environments [15–18].

At present, the frequency of occurrence and risk factors for TB infection among perinatally HIV-exposed and HIV-infected children have been largely understudied.

The aim of the study is to identify risk factors for TB infection among perinatally HIV-exposed and HIV-infected children for the further development of corrective actions.

Materials and methods

The prospective cohort study was aimed to identify risk factors for TB infection by analyzing medical records (Form 025u) of 216 children having a perinatal exposure to HIV and absent virus transmission as well as medical records of 121 children with HIV infection, including 61 children with coinfection (HIV + TB). All of them underwent regular medical check-ups at the clinical and diagnostic department of the Regional Center for AIDS Prevention and Control.

The inclusion criteria for the study enrollees were as follows: regular medical checkups, Ekaterinburg residency and perinatal infection. The exclusion criteria included residency outside Ekaterinburg and other routes of infection.

A total of 281 medical charts of the parents were analyzed to estimate the degree of exposure in the TB-affected households where the children lived.

The control group was composed of 100 children born to HIV and TB-negative mothers at maternity hospitals in Ekaterinburg.

The mean age of the HIV-exposed children at the time of study was 3.9 ± 2.7 years (95% confidence interval (CI) 9.1–1.4), HIV-infected children — 8.8 ± 0.5 years (95% CI 19.7–1.4) and the control group — 2.4 ± 0.3 years (95% CI 2.9–1.8).

CD4-lymphocyte counts were measured at the time of clinical diagnosis to assess the immune status of the HIV-infected children. The assessment of immune disorders in the respective age groups was performed in compliance with Clinical Guidelines No. 459, HIV Infection in Children, which were adopted by the Ministry of Health of the Russian Federation in 2017 (for children under 5 years of age — by CD4 percentage; for children older than 5 years — by absolute CD4-lymphocyte count).

The study included epidemiological (descriptive, evaluative, and analytical) and statistical research methods. The statistical analysis of the obtained data was performed by using Microsoft Excel 2016 and Statistics 23.0 software programs (IBM SPSS Statistics). Computations included the arithmetic mean (M), standard error (*m*), mean squared deviation, and the median (*Me*). The study validity was verified with the help of Pearson's chi-squared text (χ^2), Student's t-test (*t*), and the Fisher angular distribution (φ). The risk factors for TB development in HIV-infected children were assessed with the odds ratio within the 95% CI. For perinatally HIV-exposed children, we used the univariate analysis to assess the relative risk (RR) of tuberculosis development. The logistic regression analysis with a stepwise variable selection option was performed to identify independent risk factors. The statistical significance was set at $p < 0.05$.

The study was approved by the local Ethics Committee of the Ural State Medical University (Approval No. 9 dated 18.11.2018). The parents signed their informed consent to have their and their children's personal data processed.

Results

In the group of perinatally HIV-exposed children, 73.8% of children were born to two-parent families, in more than fifty percent of which both parents were HIV-positive (**Table 1**).

In 17 TB-affected households with parents having TB, 22 children were in household contact. More than half of the parents with TB disease belonged to TB care Group 1. The TB prevalence among the fathers was 1.9 times as high as among the mothers (8.5 ± 2.6% compared to 4.4 ± 1.6%; $p > 0.05$).

In addition to TB, some of the parents were bloodborne hepatitis virus carriers and continued using injection drugs. The hepatitis attack rate among mothers was 30.0 ± 3.6% and was 2.2 times higher than among fathers — 13.6 ± 3.2% ($t = 3.4$; $p < 0.05$). Mothers used injection drugs slightly more often than fathers (21.3 ± 3.2% compared to 17.8 ± 3.5%; $p > 0.05$).

The occurrence frequency for TB-affected households among concordant and discordant couples was highly different, amounting to 19.5% compared to 4.9%, respectively ($\varphi = 2.4$, $p < 0.01$). In households where both parents were HIV infected, active TB was diagnosed in 60% of parents, while in household with one HIV-infected parent, it was diagnosed in 50%.

When assessing the risk of TB development in households of discordant and concordant couples, it was found that in households where both parents were HIV-infected, the children's possibility of TB disease following infection was 5.3 times higher than in households with HIV-discordant couples (RR = 5.3; 95% CI 1.7–21.7; **Table 2**).

The household TB contacts differed in BCG vaccination coverage and timing patterns. In the households with discordant couples, all children were vaccinated against TB, though not always on schedule. In the households with concordant couples, 90% of children were vaccinated; however, only a third of them were vaccinated at maternity hospitals, while the other two

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Table 1. Characteristics of children in the studied groups

Analyzed parameters	Children exposed to HIV (*n* = 216)		Coinfected children (HIV + TB) (*n* = 61)		Children with HIV infection (*n* = 60)		HIV-negative children (*n* = 100)	
	abs.	%	abs.	%	abs.	%	abs.	%
Parents	160	100	61	100	60	100	100	100
Couples	118	73,8	51	83,6	45	75,0	100	100
No father	42	26,2	10	16,4	15	25,0	–	–
Concordant pairs	77	65,3	37	72,5	30	66,7	–	–
Discordant couples	41	34,7	14	27,5	15	33,3	–	–
Father is an injecting drug user	21	17,8	15	29,4	10	22,2	–	–
Mother is an injecting drug user	34	21,3	14	23,0	12	20,0	–	–
Mother and father are injecting drug users	19	16,1	9	17,6	7	15,6	–	–
Father with viral hepatitis	16	13,6	4	7,8	3	6,7	–	–
Mother with viral hepatitis	48	30,0	15	24,6	26	43,3	2	2,0
Mother and father with viral hepatitis	30	25,4	6	11,8	4	8,9	–	–
Father with hepatitis virus	10	8,5	14	27,5	4	8,9	–	–
including those who died from TB	0	–	3	21,4	0	–	–	–
Mother with TB	7	4,4	17	27,9	6	10,0	–	–
including those who died from TB	0	–	6	35,3	0	–	–	–
Mother and father with TB	0	–	13	25,5	3	6,7	–	–
including those who died from TB	0	–	4	30,8	0	–	–	–

Table 2. Risks of TB infection in children perinatally exposed to HIV

Characteristics of families by HIV infection status	*n*	Foci of TB				Number among contact children		Of them got sick with TB	
		total		including dispensary registration groups IA and IB					
		abs.	% of couples	abs.	%	abs.	% of couples	abs.	%
Concordant couples	77	15	19,5	9	60,0	20	26,0	1	5,0
Discordant couples	41	2	4,9	1	50,0	2	4,9	–	–
Relative risk (95% CI)		4,0 (1,0–16,6)		1,2 (0,3–5,1)		5,3 (1,7–21,7)			

thirds received vaccination in the first year of life and after 1 year of age.

Some of the children (10%) were not vaccinated due to their parents' refusal of vaccines, and 1 child was diagnosed with intrathoracic lymph node tuberculosis, thus being exempted from BCG vaccination.

Considering that one of the risk factors for TB disease in children is their delayed vaccination, we analyzed time frames of BCG vaccination received by the children from the study groups, including their immune status (**Table 3**).

It was found that the perinatally HIV-exposed children, who were not vaccinated against TB at the maternity hospital, accounted for 65.7%, while the HIV-infected children accounted for 38.8%, thus 3.7 and 2.2 times exceeding the unvaccinated proportion in the control group (18%). Therefore, unvaccinated children from the study groups had a higher risk of infection as compared with the children from the control group. The HIV-infected children were 4.7 times as likely to be household contacts of TB cases as compared to HIV-exposed children (**Table 4**).

More than half of the parents of children from study groups were bloodborne hepatitis viruses carriers, including the hepatitis C virus (90%; $p < 0.001$). Unlike parents of the children from the control group, they continued using injection drugs, though no significant difference in the drug-use frequency was found in the study groups.

To estimate the significance of individual risk factors for TB disease in children, we performed a comparative analysis of 9 variables in two specially formed groups: The first group was composed of 61 children with coinfection (HIV + TB); the second group included 60 HIV-infected children without TB (**Table 5**).

The mean age of detection of HIV infection in coinfected children was 25.8 ± 3.4 months (95% CI 19.4–33.5) as compared to monoinfected children whose age of detection of HIV infection was 18.5 ± 4.1 months (95% CI 11.2–27.5), which fits well into the HIV diagnosis time frames[3]. Among the children with coinfection (HIV + TB), the HAART initiation time from the HIV infection diagnosis exceeded 8.6 times the initiation time for monoinfected children (31.1 ± 5.3 months compared to 3.6 ± 1.5 months).

The analysis showed that the most significant factors for development of TB among HIV-infected children included household TB contacts, late diagnosis of HIV infection and initiation of HAART beyond 6 months of the diagnosis when children already developed severe immunosuppression.

The obtained results were used to build a logistic model for estimation of the probability of TB development in HIV-infected children (**Table 6**).

The model building made it possible to identify 5 independent factors having an impact on TB incidence among HIV-infected children:

- contact with a TB case ($p = 0.0001$);
- late diagnosis of HIV infection ($p = 0.04$);
- severe immunosuppression at the time of diagnosis ($p = 0.004$);
- initiation of HAART beyond 6 months of the diagnosis ($p = 0.001$);
- deviant behavior of parents ($p = 0.01$).

Absent vaccination against TB in HIV-infected children was not considered a risk factor for the disease; however, the assessment of the vaccination efficacy among coinfected children in different age groups showed that in the group of children from 3 to 6 years of age, the TB incidence among the unvaccinated children was 1.7 times higher than the TB incidence among the vaccinated children (63.2% compared to 36.8%) (**Table 7**).

Table 3. Characteristics of the immune status of children with HIV infection at the time of diagnosis, Me (Q_{25}–Q_{75})

Age, years	Immune categories of children with coinfection (HIV + TB)								Immune categories of children with HIV infection							
	lack of immunodeficiency		moderate immunodeficiency		manifest immunodeficiency		severe immunodeficiency		lack of immunodeficiency		moderate immunodeficiency		manifest immunodeficiency		severe immunodeficiency	
	n	CD4, cells/μl	*n*	CD4, cells/μl	*n*	CD4, cells/μl	*n*	CD4, cells/μl	*n*	CD4, cells/μl	*n*	CD4, cells/μl	*n*	CD4, cells/μl	*n*	CD4, cells/μl
< 1	5	39,0 (36,5–39,5)	3	34,0	3	27,0	13	18,0 (4,5–21,5)	19	44,0 (37,0–50,0)	9	34,0 (32,0–35,0)	5	28,0 (26,5–29,0)	10	20,0 (17,5–21,0)
1–3	5	33,0 (31,5–46,0)	3	27,0	2	22,0	16	9,5 (0–17,5)	2	34,5	1	26,0	2	20,5	3	17,0
3–5	2	32,5	1	24,0	0	0	3	3,0	4	33,5 (28,8–37,5)	0	0	0	0	1	3,0
> 5	3	1200	0	0	1	345	1	27	1	695	1	401	1	265	1	3
Total	15	36,5 (32,3–45,8)	7	28,0 (25,0–34,0)	6	25,0 (22,0–28,0)	33	11,0 (0–18,0)	26	40,0 (36,0–50,0)	11	34,0 (31,8–35,0)	8	27,0 (21,0–28,0)	15	19,5 (15,5–20,3)

Note. Me is the median CD4 cell count, interquantile range (Q_{25}–Q_{75}) was calculated per age groups.

[3] Sanitary and Epidemiological Rules SP 3.1.5.2826-10 Prevention of HIV infection. URL: http://base.garant.ru/12184824/b89690251be5277812a78962f6302560

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Table 4. Risk factors for TB in children in the study groups

Risk factors	HIV-exposed (*n* = 216) **1**		HIV-infected (*n* = 121) **2**		Control group (*n* = 100) **3**		Pearson (*p*)	Relative risk (95% CI)
	abs.	%	abs.	%	abs.	%		
Not vaccinated at the maternity hospital	142	65,7	47	38,8	18	18,0	62,3 (p_{1-3} < 0,001) 11,0 (p_{2-3} = < 0,001)	RR_{1-3} = 1,9 (1,6–2,2) RR_{2-3} = 1,5 (1,2–1,9)
Contact with a TB patient	22	10,2	58	47,9	–	–	61,0 (p_{1-2} = < 0,001) 11,0 (p_{1-3} = < 0,001) 65,0 (p_{2-3} = < 0,001)	RR_{2-1} = 3,0 (2,3–3,8)
Mother and father are injecting drug users (**1** — *n* = 160, **2** — *n* = 121)	74	46,3	67	55,4	0	0	2,3 (p_{1-2}= 0,1)	RR_{1-2} = 0,9 (0,7–1,0)
Mother and father with hepatitis virus	94	58,8	59	48,8	2	20,0	2,3 (p_{1-2} < 0,1) 85,1 (p_{1-3} <0,001) 61,4 (p_{2-3} < 0,001)	RR_{1-2} = 1,2 (1,0–1,4) RR_{1-3} = 2,4 (2,0–2,9) RR_{2-3} = 2,5 (2,1–3,3)

Table 5. Comparative characteristics of risk factors for the development of TB in children with HIV infection

Analyzed parameters	Children coinfected with HIV + TB (*n* = 61)		Children with HIV infection (*n* = 60)		Pearson (*p*)	Odds ratio (95% CI)
	abs.	%	abs.	%		
Concordant couples	37	72,5	29	64,4	0,7 (*p* = 0,4)	1,5 (0,6–3,5)
Mother and father are injecting drug users	38	62,3	29	48,3	2,4 (*p* = 0,1)	1,8 (0,9–3,6)
Mother and father with viral hepatitis	25	41,0	34	56,7	3,0 (*p* = 0,08)	0,5 (0,3–1,1)
Household contact with TB patient	44	72,1	13	21,7	30,9 (*p* < 0,001)	9,4 (4,1–21,5)
Prevention of mother-to-child transmission of HIV	24	39,3	29	48,3	1,0 (*p* = 0,3)	1,2 (0,8–1,8)
Lack of vaccination against TB	34	55,7	27	45,0	1,4 (*p* = 0,2)	0,8 (0,5–1,2)
Diagnosis of HIV infection at the age over 1 year	29	47,5	15	21,7	6,6 (*p* = 0,01)	2,7 (1,3–5,9)
Severe immunosuppression at the time of diagnosis of HIV infection*	33	54,1	15	25,0	10,7 (*p* = 0,002)	3,5 (1,6–7,6)
The administration of HAART is started more than 6 months later after the date of diagnosis of HIV infection (*n* = 57)	37	64,9	9	15,8	28,6 (*p* < 0,001)	8,7 (3,6–21,0)

Note. Children coinfected with HIV + TB: CD4 — 11,0% (< 5 years), 27 cells/μl (> 5 years); children with HIV infection 2: CD4 — 19,5% (< 5 years), 3 cells/μl (> 5 years).

Discussion

The Sverdlovsk Region ranks among the regions with the highest prevalence of HIV + TB coinfection [4]. Based on the data from report form No. 61 "Information about HIV-Infected Population", the prevalence of coinfection was 22.1 per 100,000 population in the region in 2018 and was 2.7 times higher than the average level in the country ($8.5^0/_{0000}$). In 2004–2018, 84 cases of TB disease were recorded among the HIV-infected children. Based on the report "Data on People with Tuberculosis Disease" (Form No. 33), in 2009–2018, the incidence among the children having household contacts with active TB cases showed an upward trend with average annual growth rate of 6% and was 1.9 times higher than the incidence among adults having the similar exposure (**Figure**).

Table 6. Logistic regression coefficients

Variable equations	Regression coefficients	Root mean square error	X^2 Wald	Significance level
Vaccination against TB	–0,215	1,067	0,041	0,840
Mother and father are injecting drug users	0,184	0,883	0,044	0,835
Mother and father with viral hepatitis	–2,483	1,004	6,119	0,013
HIV concordant couples	0,504	0,813	0,384	0,535
Prevention of mother-to-child transmission of HIV	0,510	1,282	0,158	0,691
Late diagnosis of HIV infection	2,570	1,226	4,397	0,036
Household contact with TB patient	4,158	0,975	18,181	0,0001
Severe immunosuppression at the time of diagnosis of HIV infection	2,673	0,917	8,504	0,004
The administration of HAART is started more than 6 months later after the date of diagnosis of HIV infection (n = 57)	3,655	1,026	12,695	0,0001
Constant	–5,137	1,711	9,014	0,003

Note. Meaning of correct classification — 52,4; consent test value — 11,7.

The probability of TB infection in children from HIV-affected households is high due to social and epidemiological factors.

The study of TB risk in children (meta-analysis), which was conducted in the United States, demonstrated that HIV-infected children were more vulnerable to TB disease following infection (OR 2.80; 95% CI 1.62–4.85) [12]. Studies conducted on the African continent confirmed that the number of TB and HIV pediatric cases in sub-Saharan African countries exceeded the numbers recorded in other regions of the world; as a result, in 2019, WHO declared the region the world's most TB/HIV burdened region (86% of TB patients had HIV antibodies)[4].

In their studies, Yakovlev et al. demonstrated that the risk of TB disease in perinatally HIV-infected children is 42 times as high as in children born to HIV-negative mothers [19].

The data from foreign researchers show that from 30 to 50% of HIV-infected children contracted TB infection through household contacts with adults (parents, grandparents) having TB infection [8]. Eremenko et al. found that the main risk factor for TB development in children was their contact with a TB case, and the HIV-infected children had the exposure rate twice as high as compared to HIV-negative children — 80.76 and 42.0%, respectively [20].

In our study, the analysis of the risk factors of TB infection among perinatally HIV-exposed and HIV infected children also showed that the rate of their TB exposure was higher than among the children of the control group, thus being consistent with the data obtained by other researchers [8, 20].

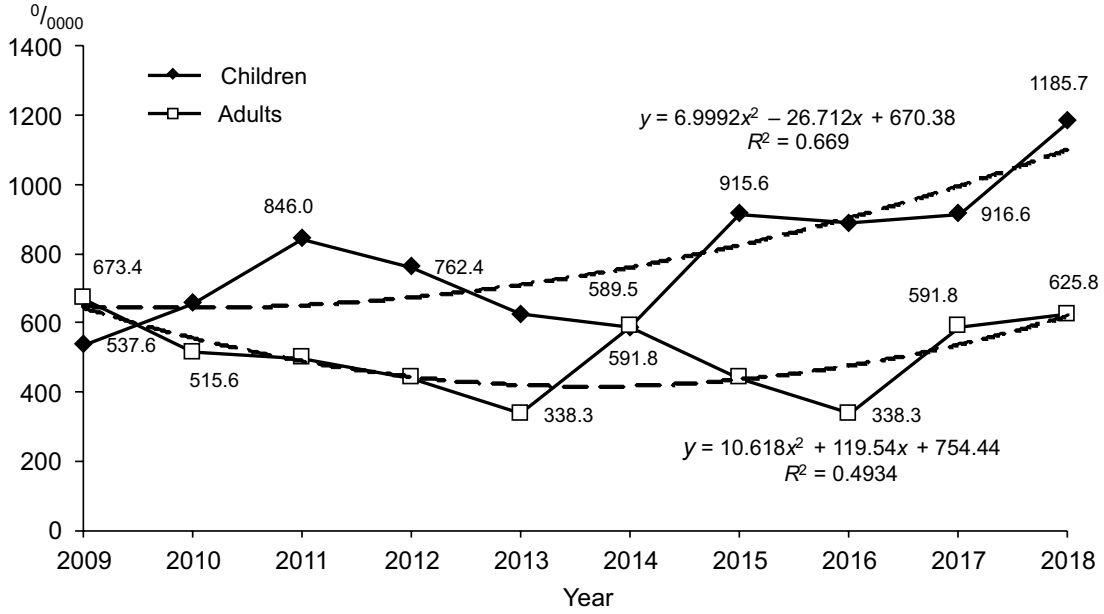
Table 7. The incidence of TB in children with HIV infection in certain age groups

Age, years	All children	Vaccination against TB			
		vaccinated		non vaccinated	
		abc.	%	abc.	%
< 1	3	0	0	3	10
1–2	18	11	61,1	7	38,9
3–6	19	7	36,8	12	63,2
7–14	20	15	75,0	5	25,0
15–17	1	1	100	0	0
Total	61	34	55,7	27	44,3

The parents of children from the study groups, unlike the parents of children from the control group, had a low level of social responsibility, as they continued using injection drugs and were carriers of bloodborne hepatitis viruses, contributing to unfavorable environments and TB spread. Our results support the studies conducted in St. Petersburg, where parental substance abuse was recorded for 85% of TB/HIV-coinfected children compared to 22% of children in the HIV-uninfected group (p = 0.02) [21].

In our study, the HIV-infected children had household TB contact 4.7 times more frequently than the perinatally HIV-exposed children ($p < 0.001$). The risk factors of TB development in perinatally exposed children

[4] WHO. Tuberculosis fact sheet, October 14, 2020. URL: https://www.who.int/ru/news-room/fact-sheets/detail/tuberculosis



Morbidity of contact children and adults in the foci of TB in the Sverdlovsk region in 2009–2018.

included living in a TB-affected household where both parents were HIV-infected (RR 5.3; 95% CI 1.7–21.7) and absence of BCG vaccination. It was found that the risk of TB infection was 1.7 and 1.9 times higher in the study groups for children who had not been vaccinated against TB at maternity hospitals as compared to the children from the control group.

It has been proved that in HIV-infected children, the resistance to TB infection depended on the initial level of immunosuppression, on progression of HIV infection and on its stage [22]. In her study of clinical progression of TB in HIV-infected children in the Sverdlovsk Region in 2004–2012, N.V. Eismont showed that the probability of TB development among HIV-negative children was lower than among children with late stages of HIV infection ($p < 0.001$) [9].

In our study, one of the independent factors of TB development in HIV-infected children was a late diagnosis of HIV infection and late initiation of HAART when severe immunosuppression was already developed. The comparative analysis of immune disorders diagnosed in HIV-infected children demonstrated that the percentage of children with profound immune deficiency in the coinfected group was 2.2 times higher and amounted to 54.1% compared to 25.0% in the monoinfected group, thus supporting the findings of other researchers. In their meta-analysis that included data of 64 cohorts of TB and HIV-infected children, Dodd et al. concluded that TB incidence was 5 (95% CI 4.0–6.0) times higher in children with severe immunosuppression compared with non-significant one [12].

The study conducted in the Primorsky Krai found that among perinatally HIV-infected children having TB, most of the children had stage 4A (61.2%); 23.5% of children had stage 4B, while the stage 4 patients accounted for only 6% in the cohort of children without TB [19].

Our study has found that earlier initiation of HAART after TB diagnosis reduces the risk of TB infection 2.1 times, which is confirmed by other studies. It was proved that among HIV-infected children receiving HAART, the incidence of TB was lower (RR = 0.30; 95% CI 0.21–0.39) than among children not receiving HAART [12]. After initiation of HAART, the TB incidence decreased within 12 months to RR 0.10 (95% CI 0.04–0.25) [12].

Conclusion

Risk factors for TB development among perinatally HIV-exposed children are household contacts with active TB, parental HIV concordance and delayed or absent vaccination against TB.

Predictors of TB disease among HIV-infected children can include a household TB contact, late diagnosis of HIV infection, severe immunosuppression, initiation of HAART later than 6 months after the confirmation of diagnosis, and deviant behavior of parents.

The most essential corrective measures are early diagnosis of HIV infection and timely initiation of HAART as well as isolation from the source of infection and timely vaccination against TB in accordance with the National Immunization Schedule of the Russian Federation.

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