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MODERN STATE OF THE PROBLEM HIV/AIDS IN CHILDREN

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Abstract. *Every day, the number of HIV-infected children around the world is increasing, mainly through vertical transmission in utero, during childbirth or in the postnatal period through breastfeeding. Also, one of the most important reasons is the lack of antiretroviral therapy in HIV-infected pregnant women, which can prevent transmission of the infection to the child.*

Keywords: *HIV, AIDS, HIV/AIDS, human immunodeficiency virus, acquired immunodeficiency syndrome.*

According to WHO, as of 2019, 8 million children under the age of 14 were diagnosed with HIV infection around the world, and unfortunately, today, 150,000 new cases of HIV infection among children are still detected annually, despite that in developed countries, with the help of antiretroviral therapy, vertical transmission of infection is reduced by an average of 52%. Of these 8 million children, almost more than 70% live in sub-Saharan Africa and an estimated 160,000 children in these countries became infected with HIV in 2021 [2,3,7,9].

According to other authors regarding antiretroviral therapy, the risk of mother-to-child transmission of HIV can be reduced by prenatal antiretroviral therapy, which reduces the viral load of the pregnant woman, and by this the risk of transmission can be reduced from 40% to 2%, and they also write that in In Brazil, the prevalence of HIV infection among pregnant women is relatively low, amounting to about 1% [1,4,5,6,8]. However, according to other sources, over the past 10 years, the incidence of perinatal mother-to-child HIV infection reported in Brazil ranges from 1.6% to 9%.

It has also been hypothesized that the placenta itself may also provide a barrier against vertical infection, which may reduce the risk of infection, but there is no evidence that a barrier can completely prevent HIV transmission, and the authors also believe that the last 14 days of the prenatal period is the most risky window for intrauterine transmission of infection [10,11,12].

The authors also state that at any time during lactation during breastfeeding, the risk of transmission of infection is extremely high, which is associated, firstly, with the mother’s viral load, as well as with infectious or non-infectious mastitis, through which infected cells can enter through the oral cavity and child's intestines [13,14].

Thus, measures to prevent prenatal HIV infection are early diagnosis, correct selection and administration of antiretroviral drugs, tactics for introducing periods from pregnancy to delivery, as well as the postoperative period and exclusion of breastfeeding.

The pathogenetic manifestation of HIV infection in children is associated with the interaction of the infection with the child’s body, and also has a number of factors. In principle, the pathogenesis of HIV in children has some similarities with adults, but there are a number of differences [13,14,15]. Firstly, the immunological shift has different directions, such as perinatal HIV infection affects the immature immune system, and as a result of the lesion, various embryos and fetopathies appear in the fetus, as well as dysmorphic syndrome, which marks the ambiguous manifestation of the clinical picture of HIV infection in the newborn. Secondly, children with HIV

infection are characterized by early failure of the immune system, which is explained by repeated bacterial infections, which have a special course and can be fatal.

Due to insufficient functionality of the immune system, the child's body cannot provide humoral protection against antigens. One of the insufficiencies of the immune system is hypogammaglobulinemia, in which the content of total gammaglobulins exceeds the norm and leads to a decrease in the production of antibodies in response to new antigens. Also, the progression of HIV infection leads to a decrease in levels of HIV-neutralizing antibodies and a decrease in interferon production.

Some children may have an asymptomatic course of HIV infection, because of this it is very important to know about the status of the types of the course and about changes in the immune status at different ages in children.

Currently, most authors have come to the conclusion that the rate of progression of HIV infection in children is associated with a number of factors, such as the rate of replication, that is, the characteristics of the virus itself, as well as the genetic resistance of the body, the formation and functioning of the immune system, etc. [10, 12.15]. In addition, it was found that in 71–84% of children with HIV infection, the disease progresses slowly.

The clinical picture of HIV infection in children mainly manifests itself in the first 4–5 years of life, and in 10% of infected children the disease occurs without symptoms until the age of 10 years. A rapidly progressing course of HIV infection is observed in 20–30% of children, and symptoms in these children appear from 3–5 months of life. The symptoms observed are mainly lymphadenopathy, viral-bacterial infection, anemia, the child is often stunted and there is insufficient weight gain, lethargy, swollen lymph nodes, in addition, with late detection of HIV infection and the absence of chemoprophylaxis, patients experience progressive disorders of the immune system, which manifests itself in the form of encephalopathy, pneumonia, otitis, skin disease, candidiasis and exacerbation of herpes, cytomegalovirus infection, toxoplasmosis, bacterial sepsis and others, which can be fatal.

In addition, studies by Vanyarkin et al. revealed that the majority of children born with HIV infection who did not receive antiretroviral prophylaxis had intrauterine infection affecting the lungs in 56.7%, the gastrointestinal system in 18.9%, the nervous system in 8.1%, skin in 8.1%. According to most authors, children with perinatal HIV infection have an increased risk of mortality in the perinatal period, which is associated with the immunodeficiency virus and the morphofunctional immaturity of the child, prematurity, the presence of concomitant diseases, insufficient medical care and incorrect tactics, as well as feeding characteristics.

Early detection of HIV infection in children at an early age is based on virological analysis, since serological tests are not sufficient and reliable due to insufficient sensitivity and specificity for maternal and infant antibodies. In addition, virological analysis is very useful in late stages of HIV infection, in which specific antibodies are not sufficiently produced. Also, when diagnosing, many important factors are the timing of infection, that is, the time of transmission of infection from mother to child. To reduce mortality and increase the life expectancy of HIV-infected children, early detection of HIV infection and proper prescription of antiretroviral therapy are necessary.

Virological analysis of HIV infection in children is based on the detection of genetic material or antibodies, which is carried out depending on the age of the child. Accordingly, antiretroviral therapy is carried out on the basis of confirmation of the diagnosis of HIV infection,

and the decision to use therapy is based on the state of immunological, virological parameters and the content of CD4 T-lymphocytes in the peripheral blood. Under the supervision of clinical and laboratory research, complex therapy using antiretroviral drugs is carried out. During treatment, assessment of the effectiveness and safety of the drug may be the basis for changing the drug itself or the dose.

Correct use of antiretroviral therapy in children with HIV infection leads to maximum and reliable suppression of HIV infection in the body, which allows the formation and restoration of the immune system and prevents the progression of the disease, improving the duration and quality of life. The following antiretroviral drugs are used to treat HIV infection in children: reverse transcriptase inhibitors, nucleotide and non-nucleoside reverse transcriptase inhibitors (ddidanosine, stavudine, phosphazide, nevirapine, efapirenz), HIV protease inhibitors (Atazanavir, Indinavir, Ritonavir, fosamprenavir), fusion inhibitors (enfuviritis), HIV integrase inhibitors (retrogravir) [15]. Also, more than 30 antiretroviral drugs are currently approved in the United States, but the pharmacology, efficacy, and safety of these drugs are not well understood and therefore they are used very off-label.

In all HIV-infected children receiving antiretroviral therapy, the focus is on the presence of clinical and laboratory manifestations of drug toxicity or intolerance. According to the authors' research, it was found that 24.7% of newborns had digestive system disorders and 59.7% had enteropathy, mainly in premature infants.

Also, based on the work of other authors, the following side effects of antiretroviral therapy have now been identified: peripheral neuropathy, hyperglycemia and insulin resistance, hepatotoxicity, lactic acidosis, pancreatitis, osteopenia and osteoporosis, anemia, thrombocytopenia, as well as skin rashes and hypersensitivity reactions. In addition, children with HIV infection require antiretroviral therapy for longer periods of time than adults for effective treatment.

WHO recommendations on the use of antiretroviral therapy have been revised five times over the past year, and each time the criteria for choosing treatment have been relaxed, and the age of immediate use has been raised. Also, in a study by most authors, it was revealed that the majority of deaths among young children with HIV infection were mainly observed in the group of children with late initiation of antiretroviral therapy and among untreated children.

According to Forrestel (2016), skin diseases occur in 78–89% of HIV-infected children and, unlike specific skin diseases, in HIV-infected people, skin pathology mainly manifests itself in severe form, with the participation of cardiovascular, endocrine and musculoskeletal diseases. systems, they are also difficult to treat.

Also, Sabyasachi (2012) reports that dermatological diseases occurred in 90% of patients with HIV infection and publications note that some dermatological problems (seborrheic dermatitis, oral candidiasis and herpes zoster) may be indicators for the early diagnosis of HIV infection, and are also an indication for preventive therapy of other dermatological diseases.

In HIV-infected children, skin diseases may manifest differently, depending on the severity and relationship with other infectious diseases. Infectious skin lesions in children with this pathology have a general connection with the state of the child’s immune system at the stage of HIV infection, and the course and manifestations of non-infectious skin lesions have not been sufficiently studied. In addition, skin diseases are the most common pathology in children with

HIV infection. There is also evidence that skin diseases in HIV-infected children are more common in boys.

The cutaneous immune system is unique relative to other organs in that the skin has two types of antigen-presenting cells (Langerhans and dermal dendritic cells), which, by activating T cells and with other cells, coordinately fight bacterial, viral or parasitic infections. And in patients with HIV infection, there is a decrease in the number of Langerhans and dermal dendritic cells, and there is also a decrease in their function.

Skin diseases in patients with HIV infection are mainly divided into two types, classified as primary and secondary skin diseases, that is, non-infectious and infectious. In addition, neoplastic skin diseases such as Kaposi's sarcoma, T-cell lymphoma, basal cell carcinoma, and squamous cell carcinoma are observed in patients with HIV infection (Table 1).

Table 1. Classification of skin pathology associated with HIV

primary manifestations	secondary manifestations	
Infectious		
seborrheic dermatitis xerosis Atopic dermatitis Eosinophilic folliculitis psoriasis itching associated with HIV 1 Medication	Simple herpes Chicken pox VPCH infection Molluscum contaginosa Infection S.Aureus Folliculitis Bullous impetigo Ecthyma Microbakterial skin infection Batsillar angimatosis Skin infection P.earoginosa Candidosis Dermatofitnious infection Gistaplasmos Kriptokokos Pneumositis pneumonia	Kaposi's sarcoma T cell lymphoma Basal cell carcinoma Squamous pack

Bereket Duko et al reported that in children with HIV infection, the most common skin diseases were fungal (49%), followed by bacterial (25%) and inflammatory (36%) skin diseases. Also, their results are consistent with the results of studies conducted in India. Sanjith and the authors also report in their works that according to the results of their study, the most common skin diseases in HIV-infected children were diffuse pigmentation of the nails, which they noted was unique in their studies, unlike others, in which the most common ones were generally shown infectious dermatoses.

Most skin diseases in HIV-infected children are similar to dermatoses in uninfected children, and also in the initial stages of HIV infection, due to progressive immunosuppression, the manifestations of skin diseases become more noticeable and widespread, in addition, they become difficult to treat.

Candidiasis or thrush is the most common mucocutaneous manifestation in HIV-infected children, estimated to be 20–72%. Candidiasis usually occurs in most infants under 6 months of

age who are not infected with HIV and is mainly caused by antibiotic therapy. The difference is that in HIV-infected children, candidiasis is observed even after 6 months of age, with relapses and a severe course accompanied by lymphadenopathy and splenomegaly.

It should be noted that candidiasis in HIV-infected children is mainly observed in the oral cavity and can be pseudomembranous, erythematous (atrophic), papillary (hyperplastic), etc. In recent studies, it has been reported that atrophic candidiasis is more common than other types in the oral cavity. Oral candidiasis is difficult to treat in HIV-infected children, and relapses are high after treatment is stopped. One of the main goals in the treatment of oral candidiasis is to prevent the spread of the disease into the esophagus. In addition to the oral cavity, candidiasis can spread through papules and pustules, affecting the folds of the neck and armpits, and in severe cases, the lesions can be completely granulomatous. Candidiasis of the nails is also quite common and is mainly observed between the ages of 2–6 years and is usually associated with nail dystrophy.

Skin fungal diseases in the form of dermatophyte are relatively rare, but the infection occurs aggressively, and with the duration of the disease, many develop an atypical form of dermatophytosis. Although most of the course of dermatophyte is common, fungal infections can provide favorable conditions for the penetration of bacterial infections.

Herpes zoster in children with HIV infection is also common, and the lesions may be erythematous and scaly, but sometimes the lesions may be atypical, such as discrete papules. The human mucosa and skin are the very first barrier, and are also one of the first indicators of systemic pathologies, including HIV infection. Also, the degree and type of skin damage can be a marker of disease progression. Worldwide, in more than 35% of children, skin pathological manifestations are counted as a symptom of HIV infection. As HIV infection progresses, a child's skin diseases become more severe and multiple, and in turn, they are difficult to respond to traditional treatment. HIV-infected children have an increased susceptibility to bacterial infections, and accordingly, the most common infection is bacterial. Treatment for bacterial skin infections will depend on the type of pathogen as well as the clinical presentation. Bacterial skin infections, especially gram-negative pathogens, can be dangerous in children and HIV-infected children. This type of skin infection requires immediate specific treatment using antimicrobial drugs to prevent meningitis and sepsis. For mild forms of bacteriological skin infections, oral antibiotics are prescribed with careful observation, in which the duration of treatment is usually longer than in uninfected children. For recurrent bacteriological skin infections, the use of a broad-spectrum antibacterial and bactericidal ointment has proven to work well, and one of them is Mupirocin. To prevent severe and recurrent bacteriological skin infections, it is recommended to use immunoglobulins for intravenous administration. Hashem in his work showed a decrease in bacteriological skin infections in HIV-infected children with the use of immunoglobulin and cotrimoxazole.

In skin diseases caused by Bartonella henselae, the main thing needs to be differentiated from Kaposi's sarcoma, which is carried out by histological examination. Patients with this skin disease without infection of internal organs and without bacteria are well treated with 8-12 days of therapy with erythromycin or doxycycline. It should be noted that bacterial skin diseases caused by Bartonella henselae are resistant to penicillin and cephalosporins. Children with HIV infection have an increased risk of developing tuberculosis not only because of their immune deficiency, but also because many of them live with adults who are HIV-infected and also infected with tuberculosis.

All HIV-infected children should receive antiretroviral therapy from birth and throughout life, as there is no specific treatment or cure for HIV. Chronic antiretroviral therapy also helps reduce various skin diseases in HIV-infected children, but there is a cumulative drug toxicity that increases the risk of developing diseases such as diabetes, cardiovascular disease, and skin drug reactions.

Antiretroviral therapy is also widely used in HIV-infected children with Kaposi's sarcoma as chemotherapy, but there are no specific recommendations. An accurate diagnosis for Kaposi's Sarcoma requires histological examination, which is not always available in undeveloped countries and the diagnosis is often based on clinical criteria. In the treatment of Kaposi's Sarcoma in HIV-infected children in insufficient conditions, liposomal drugs, anthracyclines and paclitaxel are used. And under more sufficient conditions, combination chemotherapy with non-liposomal drugs is used for treatment. Also, the use of radiation therapy and chemotherapy is possible. The use of chemotherapy for the treatment of Kaposi's Sarcoma in HIV-infected children has significant side effects, mainly in the form of toxicity, and this therapy is also high in cost and there are insufficient specialized centers that provide this procedure.

In addition, among viral skin infections in children with HIV infection, molluscum contagiosum is quite common and, with treatment, manifests itself in persistence and frequent relapses. Also, antiretroviral therapy for this pathology is the main treatment. Cryotherapy, trichloroacetic acid or 5-aminolevulinic acid are also used. For severe skin lesions, surgical excision of the affected skin area is performed.

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