

Elimination Opportunities of HIV Transmission from Mother to Child in Kyrgyz Republic

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Abstract

This article is investigating epidemiological features of HIV (human immunodeficiency virus) development in Kyrgyzstan, as well as new cases of HIV-infected patients' registration including young reproductive age women, which is directly leading to increase in their pregnancies, childbirth and children with perinatal exposure to HIV. Lack of effective, timely and adequate measures to prevent mother-to-child HIV transmission (PMTCT) leads to a direct increase in the number of HIV-infected children with vertical transmission. Initially, HIV infection in children was due to nosocomial infection and in recent years due to children birth by HIV-infected women against the backdrop of a high birth rate. Improvement of measures and optimization of PMTCT programs has led to a reduction in the risk of infection to 2.7%, which indicates a high possibility of eliminating perinatal HIV infection in the Kyrgyz Republic. The article is outlining optimizing programs main stages to reduce perinatal HIV infection from the moment of registration of the first HIV-infected pregnant woman, when antiretroviral drugs (ARV drugs) were not available, to the current stage of PMTCT using highly active antiretroviral therapy (HAART) during pregnancy, childbirth, postpartum and newborn. A comparative analysis of national clinical protocols and clinical guidelines for PMTCT for 2005 to 2021 years implemented.

Keywords: HIV-infected pregnant women, prevention of mother-to-child HIV transmission, children born from HIV-infected mothers

I. Introduction

The problem of HIV infection continues to be one of the most urgent public health problems. According to UNAIDS, currently the number of people infected with HIV on Earth is from 33.4 to 46 million people, while the number of new infections annually exceeds 4 million people (Aleksandrova et al., 2005). Over

the past few years, women number has reached 50% among newly registered cases of HIV infection (Anokhin et al., 2008). Very often, women learn about their HIV status during pregnancy (Zavalco & Kotelnikov, 2016).

It should be noted that among HIV-infected women, more than 90% are women in childbearing age (Kozyrina et al., 2018; Konnov, 2011). 2.1 million children living with HIV under age of 15 were infected in utero at birth or through breastfeeding (Latysheva & Voronin, 2014; Mozaleva & Samarina, 2020).

In 2006 year, 4 million new HIV- infected people appeared in the world, among which half a million were children below 15 years old (Oleinik & Fazylov, 2016). Increase in the number of HIV infection cases in women with predominantly childbearing age and the growing importance of the heterosexual route of HIV transmission have contributed to the spread of disease among pregnant women, which increases the risk of giving birth to children with perinatal HIV infection (Kyrgyz Republic Health Ministry Order, 2005).

HIV transmission from an HIV-positive mother to her child during pregnancy, delivery, childbirth, or breastfeeding called as vertical transmission or mother-to-child HIV transmission (MTCT), which is the most significant source of HIV infection in children worldwide.

Involvement of women in the epidemic is due not only to an increase in the frequency of the sexual route of infection, but also to anatomical and biological features: a larger surface area of the mucous membranes of lower genital tract, a high concentration of HIV in the sperm of an infected partner compared to the cervico-vaginal secretion, an increasing susceptibility to infection during menstruation and in the first phase of the menstrual cycle. During sexual contact, the risk of HIV transmission from a man to a woman is twice as high as from a woman to a man (Kyrgyz Republic Health Ministry Order, 2009).

The increase in the proportion of women among HIV-infected persons, as well as the annual increase in number of births is determining extreme relevance of PMTCT. Modern PMTCT includes timely diagnosis of HIV infection and identification of high-risk factors for HIV infection in pregnant women,

ART (antiretroviral therapy) in women and children, management of pregnancy and childbirth, as well as management of a child in the first year and a half of life (Kyrgyz Republic Health Ministry Order, 2015; Kyrgyz Republic Health Ministry Order, 2017).

Improving examinations of pregnant women and determining their HIV status in the antenatal period makes it possible to timely detect maternal infection and reduce or eliminate the vertical transmission of HIV infection, as it makes it possible to implement evidence-based interventions by connecting a set of measures aimed at PMTCT (Kyrgyz Republic Health Ministry Order, 2017; Kyrgyz Republic Health Ministry Order, 2020).

The World Health Organization (WHO) has published data that even with the complete absence of medical supervision, prevention and social support, the risk of HIV transmission from mother to infant with artificial feeding is from 15 to 30%, and with breastfeeding it increases from 20 to 45% (Kyrgyz Republic Health Ministry Order, 2005; Kyrgyz Republic Health Ministry Order, 2008).

For the first time, breast milk substitutes for children born to HIV-infected mothers were recommended in 1987, since it was found that breastfeeding with milk of an HIV-positive mother increases risk of child HIV infection by 14.0% (Kozyrina et al., 2018). In 1989, researchers published data that perinatal HIV transmission can be realized antenatal, during childbirth and through breast milk with a probability from 20 to 60 % (Hoffman & Rokshtro, 2011). In the same year, it was reported that all children born to HIV-infected mothers have maternal antibodies, so a positive ELISA test does not mean that the child is infected (Borkowsky & Krasinski, 1992).

Clinical features of the HIV infection vertical transmission course in children on the example of Osh region in Kyrgyz Republic were analyzed (Bugubaeva, 2014; Bugubaeva, 2015). Analysis of HIV epidemiological situation with tuberculosis coinfection of Osh region in the Kyrgyz Republic (Abdyraeva et al., 2018) and

prevention of mother-to-child HIV transmission were performed (Motorov et al., 2020).

After successful completion of a randomized clinical trial in the United States and France, ARV drugs as a PMTCT option first recommended in 1994. Therapy included daily oral administration of the ARV zidovudine (ZDV) to the pregnant woman from 14 to 34 weeks of gestation until delivery. In addition, intravenous ZDV recommended during labor and oral administration for the newborn during the first 6 weeks of life.

This prophylactic scheme made it possible to reduce the frequency of perinatal transmission to 8.3% (Centers for Disease Control and Prevention, 1994). Further, in Tanzania, South Africa and Uganda, ARVs for PMTCT used as three short courses of combined regimens of zidavudine and lamivudine (ZDV/3TC). Within the framework of this study, the importance of initiating ART during pregnancy compared only in childbirth, the mandatory prescription of ARV drugs to a newborn child from the moment of birth established to exclude antenatal transmission of HIV infection (Cooper et al., 2002).

In 1997, in the United States, using combined HAART regimens during pregnancy, it was possible to reduce the level of perinatal transmission to 4% or less, which included ARV drugs from the group of protease inhibitors (Kyrgyz Republic Health Ministry Order, 2020). Frequency of child infection born to HIV-positive mother, as well as the development of HIV infection, depends on a number of factors: aggravated obstetric and gynecological history HIV-infected mother during pregnancy, frequency of pregnancy and childbirth in an HIV-infected woman, degree of immunosuppression, viral load, clinical stage of HIV infection in the mother during pregnancy, duration of the period of labor and choice of method of delivery, duration of breast and mixed feeding, timeliness prescribing HAART to the mother and newborn, as well as adherence to it. In addition, most HIV-contact children remain healthy, but perinatal contact can significantly affect the further development of the child after birth, manifesting itself in various disorders in

one system or another, such as the immune system, neuroreflex, etc. Therefore, not only children with perinatal HIV infection, but also HIV-negative children born to HIV-positive mothers require monitoring and correction of immunity.

Prevention of mother-to-child transmission (PMRT) was not performed only in 27.2% of cases, in the rest, starting from the 24th week of pregnancy within 4 weeks (34.3%), from 28 to 40 weeks (15.8%), and 21.5% of mothers received ART before pregnancy (Bugubaeva & Kadyrova, 2015). Thus, the trend of increasing HIV infection among women, including pregnant women and children born to them, continues. Therefore, caring for the condition of an HIV-infected pregnant woman and a child with perinatal exposure to HIV in the transmission of this infection remains an important public health issue.

2. Materials and research methods

Statistical data analyses made in the Republican AIDS Center (RC) and at Osh Regional Center for Prevention and Control of AIDS (ROCPC) for 2005 to 2021 years on PMTCT methods and children born to HIV-infected mothers. Official statistical data used for registration of HIV cases (form No. 4a), annual reports on HIV examinations (form No. 4), on HIV-positive pregnant women, children with perinatal contact for HIV and PMTCT complex (form No. 4b), dispensary observation cards for HIV-infected women and their children, as well as data from the electronic tracking system (SES) of the Republican AIDS Center and OTsPBS.

3. Results and discussion

As in the whole world, HIV infection problem remains as one of the urgent tasks for the health care in Kyrgyz Republic, since over the past years, the number of HIV-infected persons has been increasing mainly among young people of reproductive age, as well as among children who indicates the transition of

the epidemic from the environment of injecting drug users to the general population the generalized stage.

Until 1996, the Kyrgyz Republic was the only country, according to the data of the WHO Regional Office for Europe, which had no cases of HIV infection. In 1996, the first HIV infection case registered among Kyrgyz Republic citizens and continues to be one of the urgent health problems, due to its intensive prevalence mainly

among young people, high morbidity and mortality. If by 2010 year 2500 people were registered, then in 2018 approximately 7,500 people living with HIV registered in a total population of 6.1 million. As of January 7, 2021, 10,756 cases of HIV infection registered in the Kyrgyz Republic, including 598 cases among foreign country citizens. As in many other countries, there is an increase in HIV infections among young people of childbearing age as shown in Figure 1.

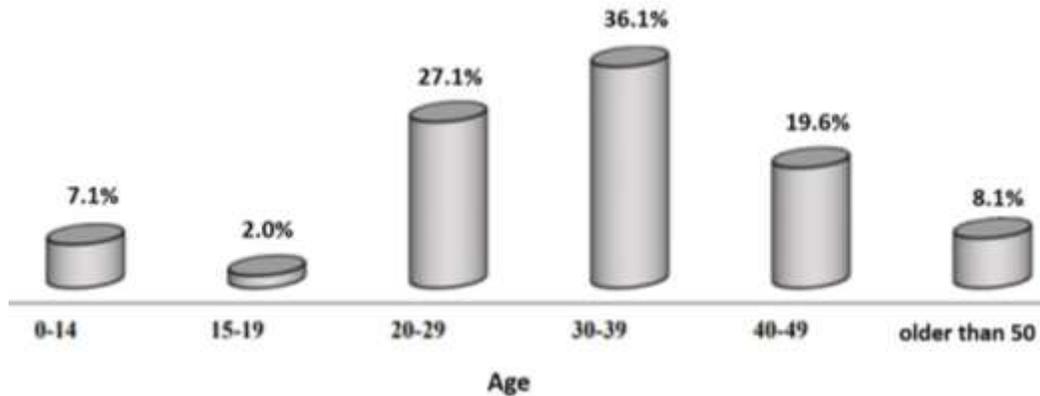


Figure 1. Age distribution of HIV-infected people in Kyrgyz Republic.

At the beginning of HIV epidemic increase in the Kyrgyz Republic, it mainly affected young men who inject drugs and unprotected sex, which subsequently involved women of childbearing age in the epidemic. Since 2005, there is a trend towards an increase in the proportion of women among registered people with HIV infection. If in 2001, HIV-infected women accounted for only 2.5%, then since 2011, their number increased to 49.0%, while

the women number among all HIV-infected people increased to 19.6 times. As of January 7, 2021, 41.4% of HIV-infected people in the Kyrgyz Republic were women, the number of which since 2009 stable over 40%. These data indicate an improvement in survey women number, including pregnant women, and a higher risk of HIV infection in women compared to men as shown in Figure 2.

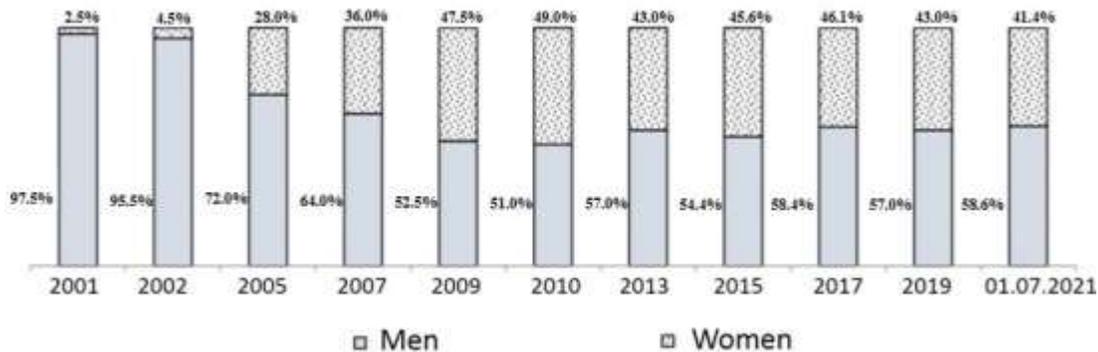


Figure 2. HIV infection cases registration among men and women in the Kyrgyz Republic from 2001 to 2021 years.

The active involvement of women is associated with an increase in the heterosexual transmission route, which leads to a direct annual increase in the number of HIV-infected women of

reproductive age in the Kyrgyz Republic and is accompanied by an increase in childbirth in this group of patients is shown in Figure 3.

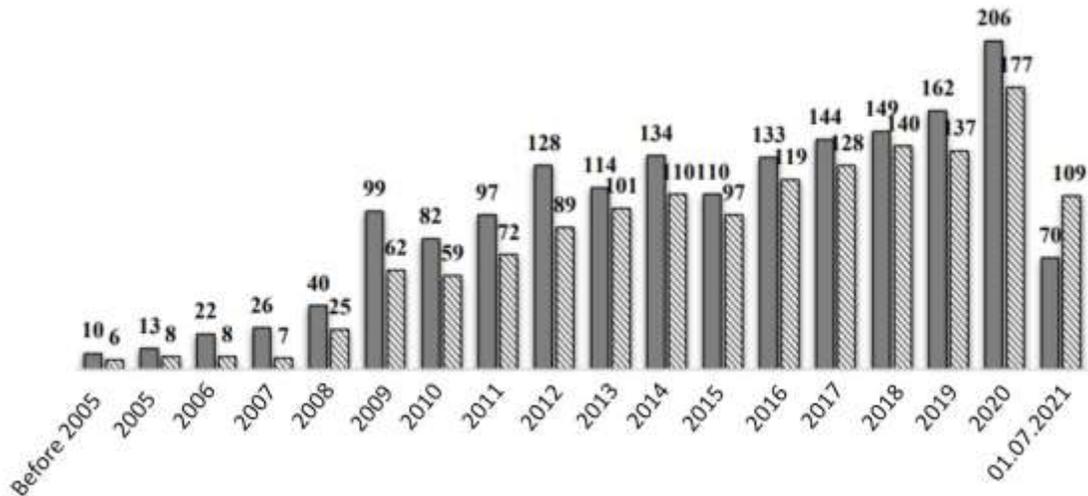


Figure 3. Dynamics of registration cases in pregnancy and childbirth among HIV- infected women in the Kyrgyz Republic from 2005 to 2021 years.

Until 2009, pregnant women were examined for HIV infection only according to epidemiological and clinical indications. Since 2009, antenatal care services have carried out mandatory HIV testing of all pregnant women, which was increased twice in 2020, during the first and third trimesters of pregnancy (Radlett, 1989). Thanks to this initiative, pregnant women number tested for HIV infection in the Kyrgyz Republic increased from 27% in 2007 to 27% up to 71% in 2008, which contributed to increase in HIV infection detection in early and late pregnancy, which makes it possible to conduct timely and more effective PMTCT measures (Centers for Disease Control, 1985).

The first HIV-positive pregnant woman in the Kyrgyz Republic was identified in 1997 in Bishkek, when registering for pregnancy. This patient gave birth naturally, ARVT was not carried out due to absence of ARV drugs in the Kyrgyz Republic in this time, and became available only since 2005. Feeding a child with perinatal contact for HIV, from the moment of birth, was carried out with breast milk substitutes. Subsequently, the child of this

patient was removed from dispensary observation with a negative HIV status.

Today, the frequency of perinatal HIV transmission in the Kyrgyz Republic is about 2.7%, which is two times higher compared with the Russian Federation and three times higher, where mother-to-child transmission of HIV is eliminated. The first country to receive the WHO vertical route HIV transmission elimination certificate in 2015 was Cuba, in 2016 were Armenia, Belarus and Moldova, in 2017 another 6 countries of the Caribbean region (Thomas et al., 1994; UNAIDS, 2020).

Approved cases of vertical transmission of HIV in children, as well as retrospective cases of the perinatal HIV infection detection determine the need for continuous improvement of measures aimed at PMTCT. Data from the United States Centers for Disease Control and Prevention (CDC), published in 1985 confirmed retrospective perinatal HIV infection in 76.0% of children, the frequency of which reached 65.0% (Costa et al., 2008). Considering the high frequency of perinatal HIV transmission, the lack of ARV drugs, high mortality of children

from AIDS in the first two years of life, all HIV-infected women of reproductive age were recommended to use reliable methods of contraception, or to terminate pregnancy if it occurs (Hoffman & Rokshtro, 2011).

Currently, to all HIV-infected pregnant women are given the opportunity to consciously decide the fate of their pregnancy; it is unacceptable to incline to terminate a pregnancy, providing full information about the risk of MTCT. Vertical transmission of HIV infection can be almost completely prevented if an HIV-infected woman receives ART during pregnancy, childbirth, and after delivery, and the newborn child receives ARV drugs after birth, as well as by the correct choice of a safe delivery method and safe method of feeding the newborn. With proper adherence to all PMTCT referrals, the risk of mother-to-child transmission of HIV is < 2% with bottle-feeding and < 5% with breast-feeding.

Currently, this is the only effective way to reduce perinatal HIV infection to a minimum level. PMTCT services provided in accordance with clinical protocol No. 917 of the Ministry of Health of the Kyrgyz Republic, developed in accordance with the recommendations of WHO/UNICEF. During introduction of PMTCT in the Kyrgyz Republic in 2007 with a single injection of ARV drug nevirapine 200 mg (NVP) during childbirth, then monotherapy with zidovudine 300 mg (AZT) was carried out from 24 to 28 weeks of pregnancy, in isolated cases, ART was performed with two (combined) ARV drugs (bithery) combivir 300/150 mg (zidovudine 300 mg/lamivudine 150 mg).

PMTCT program integration services in the Kyrgyz Republic in 2007 year allowed to minimize the risks of perinatal infection, the level of vertical transmission of HIV in 2013 was 5.1%. At the same time, according to regulatory documents, all HIV-infected pregnant women who need medical help should undergo PMTCT using combined ART. However, the timing of ARV drugs appointment depend on pregnancy timing, the clinical stage of HIV, and the level of CD4 cells. It was recommended to

start ARV drugs in pregnant women with HIV at 24 to 28 weeks with DM4 greater than 350 µL or at any gestational age with DM4 below 200 µL. Further, ARV drugs began to be prescribed from 14 to 24 weeks, considering organogenesis in the first trimester of pregnancy and the maximum effectiveness of ARV drugs until 36 to 38 weeks, since with high adherence, the viral load (VL) of an HIV-infected pregnant woman decreases below 50 copies / ml, which enables delivery in a natural way.

The main task of an HIV-infected woman is the birth of a child without HIV. Therefore, since 2015, ARV drugs have been prescribed to all identified women with HIV infection in the Kyrgyz Republic during pregnancy, childbirth and after childbirth. This method of ART is well suited for countries with high birth rates. It should be noted that in the Kyrgyz Republic more than 10% of HIV-infected women have repeated pregnancies and childbirth.

For 15 years, the country has been specifically working on a program to expand and strengthen PMTCT services for HIV-infected women and their children through the constant updating of state clinical protocols in accordance with WHO guidelines, introducing expanded HIV testing methods, modernizing laboratory capacity and adopting flexible strategies for services, aimed at improving access to and adherence to ART.

Conclusion

Since 2005 year, increase in the women number of childbearing age with HIV epidemic in Kyrgyz Republic, the increase in number of pregnancies and childbirth in this group, as well as the lack of perinatal HIV transmission elimination made it necessary for further study of this subject. Implementation of prevention mother-to-child transmission of HIV (PMTCT) complex, aimed at reducing the HIV infection risk through vertical transmission, has reduced perinatal HIV infection to 2.7%. Despite activities carried out on PMTCT in the Kyrgyz Republic, which have been updated and changed

over time based on evidence-based medicine, the frequency of perinatal transmission of HIV infection remains above 2%. To provide qualified assistance to HIV-infected pregnant women and women with HIV, it is necessary to involve not only AIDS doctors, but also obstetrician-gynecologists, infectious disease specialists, family doctors, psychologists, social workers in order to increase adherence to taking ARV drugs, monitor the effectiveness of measures aimed at the birth of healthy children.

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