

Children and Human Immunodeficiency Virus Infection

Opportunities and challenges

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الأطفال والعدوى بفيروس نقص المناعة البشري

الفرص والتحديات

مؤنس مصطفى الششتاوي

IN THIS ISSUE OF SQUMJ, YADAV *et al.* present a very interesting article about opportunistic infections and complications in children infected with human immunodeficiency virus (HIV)-1.¹ It is well known that both HIV-1 and HIV-2 progressively destroy lymphocytes, rendering the patient susceptible to a variety of other infectious agents; these infections are known as opportunistic infections.² At least 90% of HIV-infected children acquire the infection from their mothers through mother-to-child transmission (MTCT).² Approximately half of these cases occur late in pregnancy, possibly in the days before the delivery, as the placenta begins to separate from the uterine wall.³ Only a small proportion of cases (<4%) seem to occur in the first trimester, less than 20% by 36 weeks of gestation and approximately one-third during delivery.³ Many factors may increase the transplacental transmission of the virus to the fetus *in utero*, such as an increased plasma viral load; this also exposes the baby to increased concentrations of the virus in the female genital tract during childbirth. Maternal sexually transmitted diseases, Epstein-Barr virus infection, viral shedding, vaginal candidiasis and cervical inflammation are known risk factors for the MTCT of HIV.⁴ The risk of HIV transmission is also higher in cases of prolonged rupture of the amniotic membranes before delivery,³ which is usually associated with acute and chronic inflammation of the placental membranes.⁵ In spite of its importance in terms of other health benefits, breastfeeding unfortunately puts the infant at risk of acquiring HIV throughout the entire breastfeeding period, even if the infant is initially uninfected. In the absence of preventive interventions, about 5–20% of infants with HIV-positive mothers become infected through the process of breastfeeding.⁶

There is assuredly a potential benefit to testing infants for HIV infection soon after birth, i.e. before the infant is 48 hours old, so as to quickly identify infants infected *in utero* and prevent early mortality.⁷ However, certain rapid diagnostic tests, such as the current available HIV serological assays, cannot be used for diagnosis in infants below 18 months of age. This is due to the presence of maternal HIV antibodies,⁸ although these usually clear by 9–12 months.⁶ While these tests can undoubtedly be used to screen for HIV exposure among children >18 months old, a definitive diagnosis of HIV infection can only be confirmed with virological testing.⁹ In this regard, the Panel on Antiretroviral Therapy and Medical Management of HIV-Infected Children recommended two assays for virological detection: the HIV ribonucleic acid (RNA) and HIV branched deoxyribonucleic acid (bDNA) polymerase chain reaction (PCR) assays.¹⁰ Between the two, the latter is usually less expensive.¹¹ Further virological testing in infants with known perinatal HIV exposure is recommended when the infant is 14 days, one month and four months old.¹¹ Testing when the infant is 14 days old allows for the earlier detection of HIV in infants who have had negative test results within the first 48 hours of life. At the age of one month old, testing confirms the previous results, as PCR testing has a 96% sensitivity and 99% specificity for identifying HIV at this age.¹¹ Once HIV infection has been diagnosed, the course of the infection must be frequently monitored by determining the number of cluster of differentiation 4 positive (CD4+) lymphocytes (otherwise known as the CD4+ count, which decreases as the infection worsens) and the number of virus particles in the blood (also termed the viral load, which increases as the infection worsens).²

Children born with HIV infections rarely display symptoms in the first few months of life. Even without

treatment, approximately 80% of infected children do not develop problems during their first or second year.² For the remaining children, problems may not appear until the age of three years or later.² The rate of progression to a stage of clinically apparent immunosuppression depends on maternal, infant and viral factors.¹² Once this occurs, HIV/acquired immunodeficiency syndrome (AIDS) will negatively affect the children's health, education and well-being. Early signs of infection include delayed growth and recurring bacterial infections.² In a significant number of HIV-infected children, progressive brain damage prevents or delays developmental milestones, such as walking and talking. These children may also have impaired intelligence and a small head in relation to their body size.² Up to 20% of infected children who are left untreated progressively lose social and language skills as well as muscle control.²

The initiation of antiretroviral therapy (ART) in infants and children should be based on age, CD4+ count and clinical stage. An infected infant aged one year or older suffering from AIDS or showing significant symptoms of the disease should be immediately treated, regardless of the results of CD4+ percentage and count or virological assays.¹¹ For children, the drugs used during treatment are more or less the same as those used for adults—typically a combination of two nucleoside or nucleotide reverse transcriptase inhibitors (NRTIs) plus one non-nucleoside reverse transcriptase inhibitor (NNRTI) or one protease inhibitor (PI).¹¹ The effectiveness of the treatment should be monitored by regularly measuring the viral load in the blood and the CD4+ count.² Yadav *et al.* observed that the severity and frequency of opportunistic complications in paediatric patients infected with HIV-1 increased with a fall in the CD4+ count.¹ The authors hypothesised that treating the opportunistic infections, along with ART, might lead to both clinical and immunological recovery and a decreased incidence of future opportunistic infections.¹ While opportunistic infections in adults are secondary to the reactivation of opportunistic pathogens acquired when the host's immune system was still intact, opportunistic infections in children usually reflect a primary infection.⁴ Among children with perinatal HIV infection, the primary opportunistic infection occurs after HIV infection is established and the child's immune system has already been compromised. This can lead to different disease manifestations than those witnessed among adult patients.⁴

In general, HIV treatment should continue indefinitely, or at least until the child is five years old, though it may sometimes be stopped following the

successful completion of ART.¹³ It is important to mention here that treating infected children is not an easy task. Some of the drugs used to treat adult patients, which are not in liquid form, are not suitable for infants and young children. Complicated drug regimens can also limit the effectiveness of chosen therapies as they may be difficult to follow for both parents and children in the long term.² Additionally, the side-effects of certain drugs, though better tolerated by children in comparison to adults, may also limit the treatment of HIV-infected children.²

Current advances in HIV treatment are changing the pattern of HIV/AIDS in clinical settings. Prior to effective antiviral suppressive therapies, the majority of HIV-infected infants developed marked immunosuppression and AIDS-defining conditions at an early age. Today, ART makes it possible for children to experience prolonged viral suppression and live well into their adolescence and early adulthood.¹⁴ The prognosis is worse for those in whom the virus is detected within the first week of life or for those who develop symptoms in the first year of life.²

The latest report by the United Nations Children's Fund explores the strides that have been made in the fight against HIV.¹⁵ In this report, more than 850,000 children in low- and middle-income countries, whose mothers were living with HIV, were estimated to have been born without contracting the infection between 2005 and 2012.¹⁵ However, despite the progress achieved, there is still a long way to go—in 2012, around 260,000 children in low- and middle-income countries were newly infected with HIV and during that year almost 600 children died from AIDS-related causes every day.¹⁶ As stated by Yadav *et al.*, HIV infection is rapidly increasing among the paediatric HIV population in India and, with the current rate of increase, India will soon have the highest AIDS prevalence worldwide.¹

In the Middle Eastern and North African (MENA) region, the HIV epidemic has been rising since 2001. This region is currently among the top two regions (along with sub-Saharan Africa) in the world with the fastest growing HIV epidemics.¹⁷ The number of children younger than 15 years living with HIV and those newly infected with HIV in the region is increasing.¹⁷ Also, ART coverage in the region remains one of the lowest in the world. In 2010, the percentage of pregnant women receiving the most effective antiretroviral regimen for the prevention of MTCT was less than 5% and the percentage of infants exposed to HIV who received antiretroviral prophylaxis was only 2%.¹⁷ HIV-related stigma and discrimination are no doubt still rife in the MENA region and these are major barriers to the utilisation of HIV-preventive

services. Accordingly, the use of counselling and testing services is generally low; it may be even lower for women, given the prevailing cultures and traditions of this region.¹⁷ Moreover, women with an increased risk of contracting HIV suffer from a lack of services that are adapted to their needs. There is an inadequate understanding of the vulnerability of women who do not themselves engage in high-risk behaviours but are nevertheless exposed to HIV infections.¹⁷ One encouraging sign in the MENA region is in the case of Oman, a nation which has demonstrated an acceptance of HIV-specific screening interventions despite the inherent cultural sensitivities of this topic. In 2009, Oman offered HIV testing to all women attending antenatal care clinics, with 99% of them opting for the test.¹⁷ Furthermore, the percentage of ART coverage recorded in Oman was the highest in the region (78%), followed by Morocco (26%).¹⁷

In recent years, the global efforts expended to combat HIV/AIDS have increased, with an accelerated global commitment to the prevention of MTCT. For instance, the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organization (WHO) introduced a new initiative in June 2010 aiming to achieve and sustain universal access to ART and maximise the benefits of different HIV-preventive interventions through focused work in five priority areas.¹⁸ One important priority area is to provide HIV testing nearer to the point-of-care (POC).¹⁸ This is particularly important because new innovations such as simplified virological testing make it possible to provide an earlier diagnosis for infants closer to the POC and facilitate the introduction of rapid and integrated treatment.

In 2011, the United Nations hosted a High-Level Meeting on AIDS in New York, in which the General Assembly adopted the Political Declaration on HIV/AIDS.¹⁹ One of the targets of this declaration was to eliminate the MTCT of HIV by 2015.²⁰ In this instance, elimination is defined as a 90% reduction in the number of new paediatric HIV infections, or a MTCT rate of below 5%.²⁰ All nations will have to show great dedication to achieving this target as the deadline approaches. The WHO validation requirements for this elimination are based on documented evidence on the achievement of the elimination targets for at least three consecutive years, the existence of an adequate surveillance system and evidence of each programme's capacity to sustain the elimination targets and objectives in the future.¹⁷

Crucially, sustained national commitment, sufficient human and financial resources and the delivery of critical interventions are key points for the success of any programme aiming to eliminate

the MTCT of HIV. Interventions should focus on simplifying and enhancing accessibility to treatment and other services for pregnant women living with HIV and on relieving the suffering of those most afflicted by the epidemic. With all these factors in hand, an HIV/AIDS-free generation may well be within reach and will be a strong foundation for a better future.

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