

An Update on HIV and Pregnancy

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Highly active antiretroviral therapy has dramatically reduced morbidity and mortality in human immunodeficiency virus (HIV)-positive patients, turning the disease into a chronic manageable condition. The risk of HIV transmission from mother to child is lowered to about 1% when interventions are maximised. The universal antenatal HIV testing programme introduced in 2001 has proven to be an efficient and effective initiative in Hong Kong. Introduction of rapid testing for late-presenting mothers with unknown HIV status will add to its success. It is becoming ever more important to fully address the reproductive needs of HIV-positive women and their spouses, aiming at safer sex practices, the use of safe and reliable contraception, the delivery of healthy babies after planned pregnancies, and prevention of HIV transmission.

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Background

Acquired immunodeficiency syndrome (AIDS) was first reported in 1981 in the United States¹, followed by the discovery of its causative agent—the human immunodeficiency virus (HIV) 2 years later. Since then HIV/AIDS has spread to nearly all territories of the world and led to unprecedented health and social impacts to mankind. Sub-Saharan Africa has been bearing the brunt of the global epidemic though several Asian countries also suffered from a serious epidemic. Notwithstanding a diverse HIV situation across, stigmatisation of HIV/AIDS patients is universal and Hong Kong is no exception². On the other hand, scientific and medical advances, notably the introduction of highly active antiretroviral therapy (HAART) in the mid 1990s, have significantly decreased the morbidity and mortality of HIV/AIDS and changed the clinical landscape^{3,4}.

Over the years, Hong Kong has had a low prevalence of HIV. To date, sexual contact remains the most frequent route of transmission in adult cases of HIV. Most infected children, however, acquired the virus from contaminated blood products in early 1980s or through vertical transmission from their infected mothers. While the general public in Hong Kong continues to view HIV as an uncommon condition, most consider having children to be a part of life. Many pertinent medical and social issues

may arise when HIV-positive women become pregnant. This paper attempted to briefly review selected areas of the subject with a local perspective, in the context of the latest international developments.

Mother-to-child HIV Transmission

Mother-to-child transmission (MTCT) is one of the three modes of HIV transmission and accounts for over 90% of HIV infections in children worldwide. The World Health Organization advocated prevention of MTCT via a three-pronged approach, namely (a) preventing HIV infection in reproductive-age women, (b) preventing unintended pregnancies in HIV-positive women, and (c) preventing perinatal transmission via prenatal screening and treatment of infected mothers.

Providing information on pregnancy forms an integral component of care for HIV-positive women. When pregnancy is contemplated, further counselling should be given on multiple aspects, including the effects of HIV during pregnancy on the mother and foetus, and the effects of pregnancy on HIV, how to minimise

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transmission to the baby, as well as general maternal health maintenance and the impact of pregnancy and childbirth on the woman's family. In general, CD4 cell count remains stable without enhanced disease progression when HIV-positive women get pregnant. On the other hand, there are limited data of adverse pregnancy outcomes associated with HIV, such as spontaneous abortion, low birth weights, and preterm delivery. The goals of managing an HIV-positive pregnancy are to minimise MTCT, deliver a healthy baby, maintain the well-being of the expectant mother and prepare the family to take care of the baby. Collaborative efforts of obstetricians, paediatricians, and HIV physicians are crucial.

Risk and Timing of Mother-to-Child Transmission

Compared with transmission via sexual contact and needle sharing, MTCT is a much more efficient mode of transmission. The transmission rate from HIV-positive pregnancy through delivery is estimated at 15-30%. Less than one-third of vertical infections occur intrauterine. The remainder occur during the intrapartum and perinatal period. Overall, the risk of MTCT is found to be higher in developing than developed countries. Maternal factors, eg high HIV viral load, advanced disease stage, as well as intrapartum factors, such as prolonged rupture of membranes and invasive foetal monitoring, increase the risk of transmission. Also, there is a 15% additional risk of infection from breastfeeding during the first 24 months' postpartum⁵. Hence, in developed countries where safe formula feeding is available, HIV-infected mothers should refrain from breastfeeding.

Diagnosis and Interventions of HIV-positive Pregnancy

Detection of underlying HIV infection in expectant mothers is the key to interventions to reduce MTCT. Besides, diagnosis enables early referral for HIV care of infected women and other planning relating to the disease. In the past, a selective risk-based testing approach in pregnant women was employed but shown to have missed many HIV-positive pregnancies. Hence, routine HIV screening of antenatal women is advocated to improve diagnosis of infected mothers; such screening programmes have already been implemented in different parts of the world.

As early as 1994, the ACTG 076 study found that 3-part (antenatal, peripartum and postnatal) zidovudine could reduce MTCT rate to 7.6%, as compared to

22.6% in the placebo-treated group⁶. Minimal toxicity, mainly transient anaemia, developed in mothers and infants. This landmark study offered significant hope that vertical transmission could be greatly reduced and has established a precedent for subsequent research. Subsequent studies on short-course zidovudine and the use of other antiretroviral agents in different regimens further demonstrated the success of antiretroviral prophylaxis in reducing MTCT⁷⁻⁹.

Presently, as evidenced from epidemiologic and cohort studies, HAART is the most effective antiretroviral regimen for MTCT prevention. In the best scenario, the risk of transmission is brought to 1% or below. Nevertheless, the choice of drug is important. For example, the combination of stavudine and didanosine is associated with a high risk of fatal lactic acidosis in pregnant women and must be avoided. Efavirenz is contraindicated due to its teratogenicity effect; the use of nevirapine is a concern for its high frequency of allergy in females¹⁰. The recent recall of nelfinavir due to drug contamination has made Kaletra (lopinavir-ritonavir) the first-line protease inhibitor, although both ritonavir-boosted saquinavir and indinavir are acceptable alternatives¹¹.

Elective caesarean section is effective in reducing MTCT. It is recommended if maternal viral load is >1000 copies/ml prior to delivery¹². Studies evaluating the role of elective caesarean section when viral load is <1000 copies/ml have been inconclusive. Caesarean section may also be protective in the setting of HIV hepatitis C co-infection.

Diagnosis of HIV-infected expectant mother should still be made as far as possible in peri-delivery period for late-presenting women. Suboptimal two-part⁹ or even early postnatal⁸ antiretroviral prophylaxis works to significantly decrease MTCT. Furthermore, elective caesarean section should be considered in these cases; invasive procedures, such as foetal scalp electrode and episiotomy, should be avoided. All of these are important for optimising HIV and obstetric care of infected mothers when they present late in pregnancy. Hence, in 2004 the US Centers for Disease Control and Prevention recommended routine rapid HIV testing at the time of labour or delivery for women with unknown HIV status¹³.

Hong Kong Experience

A pivotal study in 1999 found that universal HIV screening of pregnant women with an opt-out approach is practical, feasible, and clinically acceptable in Hong Kong¹⁴. This set the scene and provided local evidence for adopting a universal antenatal testing programme (UAT) in Hong Kong, which was successfully launched in September 2001. In the last 5 years, screening was widely accepted by antenatal women in public service and the opt-out rate was less than 3%. However, the proportion of women with known HIV status before delivery in public hospitals decreased from 91% in 2003 to 85% in 2006 while that in private sector increased from 72% to 95%. As of 2006, a total of 41 positive pregnancies were detected under the UAT programme. Of 34 HIV-positive pregnancies identified before delivery, 17 mother-infant pairs received 3-part antiretroviral prophylaxis and none of the babies acquired HIV. On the contrary, of seven babies with maternal infection diagnosed only after delivery, two did not receive any antiviral prophylaxis and became infected. An evaluation indicated that UAT is a cost-effective programme, though its success relies on high screening rate and the availability of antiretroviral prophylaxis¹⁵.

It is clear that UAT has helped to prevent MTCT in Hong Kong. However, a prevention gap exists for those infected women whose status was unknown prior to delivery, hampering prompt interventions to reduce MTCT. For this reason, the Advisory Council on AIDS, in its latest HIV/AIDS Strategies for Hong Kong, recommended the incorporation of rapid testing for late-presenting mothers with unknown HIV status¹⁶. With the support of Hospital Authority and the Scientific Committee on AIDS and STI (SCAS), the Centre for Health Protection, Queen Mary Hospital conducted a pilot trial from March to May 2007 to examine the feasibility and acceptance of rapid HIV testing in labour ward. The study found that this screening programme could provide rapidly available results compared to conventional HIV antibody testing, and was acceptable to both patients and health care providers. This study provided local evidence for Hospital Authority of the value of rapid HIV testing in late-presenting mothers with unknown HIV status. The SCAS has also revised its clinical guidelines to specify the most effective antiretroviral regimens to prevent vertical transmission and manage maternal infection¹¹.

Reproductive Care

Pre-conceptional health care is desirable for women of child-bearing age, irrespective of their HIV status. This would include counselling about safer sex practices, contraception, and family planning. For infected women who did not intend to conceive, advice on contraception and safe sex practices is important. Hormonal agents and intrauterine devices can augment the contraceptive effect of condoms. Drug interactions should be considered for hormonal contraceptives, especially in patients treated with antiretroviral drugs.

On the other hand, providing care to facilitate planned pregnancy is equally important but more complicated. In fact, there is evidence suggesting that an increasing number of HIV-positive women and men wish to have children^{17,18}. Given the likelihood of reduced fertility in HIV-positive patients and the risk of HIV transmission from unprotected sex for natural conception, HIV-positive couples are candidates who will benefit from assisted reproduction. Counselling is indispensable in this regard. Local and international guidelines/recommendations have been developed on the subject^{19,20}.

There are three scenarios of assisted reproduction according to the HIV status of the couple: (a) discordant couples where the woman is positive, (b) discordant couples where the man is positive and, (c) couples in which both partners are HIV-positive. Artificial insemination can be employed for positive women if their partners are negative. If conception fails after 6-12 months, infertility workup and other assisted measures such as ovarian stimulation and in-vitro fertilisation, may be needed. Sperm washing of HIV-positive man is very effective and safe in achieving conception without infecting HIV-negative women²¹. Sperm washing is also recommended for planned pregnancies in concordant positive couples.

Conclusion

The emergence of HIV/AIDS has had great implications for the practice of both medical and social science. Although a quarter of a century has elapsed, the epidemic is expected to stay with us for another quarter of a century or longer. HIV-positive women are living longer and healthier lives. The management of HIV

longer and healthier lives. The management of HIV during pregnancy represents a specific and focused area that demands attention. Advances in medical treatments, together with the increasing number of infected women wishing to have children, ensure that new debates, challenges, and inspiration are to be expected.

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