Management of HIV infection in pregnancy

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Abstract

Human immunodeficiency virus (HIV) remains an important global infection and cause of significant morbidity and mortality. The majority of new HIV infection occurs in the developing world, where women and their children are greatly affected by the consequences of HIV associated disease. By comparison, in the developed world, women represent a minority of those with new HIV infection. The problems associated with the management of pregnancy and childbirth require specialist care across multidisciplinary teams to ensure the best clinical outcome for mothers and their babies, as well as assuring the confidentiality and safety of patient care and public health. Preventing mother-to-child-transmission (MTCT) has been the goal of research and collaborative guidelines in the UK for much of the past decade and has contributed to reducing MTCT, which is now a rare occurrence in the UK. The global target of eliminating MTCT requires a major and sustained effort to improve access to testing, antiretroviral therapy and expert multidisciplinary care.

Keywords antiretrovirals; breastfeeding; epidemiology; HIV; pregnancy; pre-labour Caesarean section

HIV and women

About 33.3 million people worldwide are infected with HIV and almost half of them are women. Poverty is a major component of new infection with 98% of women with HIV living in resource poor countries. Migration to developed countries, including the UK, should be prioritized as a public health issue.

In the UK, HIV testing uptake has been successful through women attending Genitourinary Medicine clinics and antenatal clinics. However, a significant proportion (27%) of women (especially from sub Saharan Africa) are unaware of their status and present late. One third of all new HIV diagnoses are in late presenters and have a CD4 count of below 200 cells/μl (Box 1). New efforts through community testing pilots, British Association for Sexual Health and HIV guidelines and the *Halve It* campaign aim to reduce the undiagnosed fraction; with earlier therapy, this should further reduce morbidity and new transmissions.

Natural history

The majority of HIV infections are caused by HIV 1 whilst HIV 2 infections are very uncommon. HIV 2 infection occurs mostly in West Africa and has a much lower virulence and transmission.

After infection, viral replication and integration results in a gradual loss of the CD4 lymphocyte count causing immune deficiency, indicated by a cell count less than 350 cells/mm^3. This can lead to a variety of opportunistic infections or subsequently a risk of developing AIDS. The time span from seroconversion illness to AIDS is very variable; some cases develop over a few months whilst for other individuals there is minimal immunosuppression a decade or more after infection.

Management of HIV has been transformed in the past decade by effective combination antiretroviral therapy (ART). This has led to a restoration of immune competence, undetectable viral loads and improved life expectancy. The effect of ART has been to restore quality of life and increase wellbeing. ART has reduced transmission to sexual partners as well as through MTCT.

Mother-to-child-transmission

In the UK, maternal to child transmission of HIV has significantly decreased from 20% to 2% from 1993 to 1998 (Box 2); this was primarily due to a better understanding of management of HIV infection and also the prophylactic use of highly active antiretroviral therapy (HAART). The risk of transmission is highly dependent on the viral load (VL). At a viral load of >100,000 copies/ml there is a 40% risk of transmission. This falls to 1% at 1000 copies/ml and less than 1% at undetectable VL (<50 copies/ml). Management also considers the mode of delivery,

HIV in the UK. Adapted from the Health Protection Agency 2010 report

2010
91,500 people living with HIV in the UK
30,000 women
- 24% unaware of their infection
- 21% for women (antenatal screening programme ↑ detection rate)

6660 new diagnoses
- 50% heterosexually acquired

2150 women

Gradual increase in new diagnoses among people acquiring infection heterosexually in UK
2004 — 740
2008 — 1080
2010 — 1090

Box 1

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MTCT in the UK

- Approximately 1600 pregnancies and 1400 births reported each year
- 80% of pregnant women with HIV are of African origin
- 70% of pregnancies are in previously diagnosed women, many having a second or subsequent pregnancy (20%)
- Very low (<1%) MTCT rates for diagnosed women
- Of approximately 40 HIV infected children each year, only 10 are born to diagnosed women

Box 2

appropriate and timely intervention of post-exposure prophylaxis (PEP) for the infant and avoidance of breastfeeding.

In the UK, over half of pregnant women with HIV present late for antenatal care. 50% present after the first trimester compared to 22% of HIV negative women. Late presentation and later booking have adverse consequences for both mother and child and this situation can be improved with a dedicated and flexible team of specialist midwifes, obstetricians and HIV physicians, who are all in constant communication with each other.

Antenatal testing

The UK introduced routine 'opt out' antenatal HIV testing in 1999; the uptake in 2008 was 92–95%. Testing is performed at booking (12–14 weeks) and no further HIV tests are offered. As there have been a number of HIV seroconversions during pregnancy, the question of whether further HIV testing should be offered later in the pregnancy, especially in high risk groups or in ethnically diverse areas such as London is pertinent. This issue was raised by the perinatal transmission audit, which highlighted the need for health economic data to consider a second HIV test in the third trimester. In the UK, women who refuse antenatal testing do so because they believe they are at risk of HIV. This is, however, based on poor information and patchy knowledge.

It is extremely important to have a dedicated midwife/women's health advisor with close links to HIV teams who can identify high risk pregnant women and offer subsequent tests, educate and arrange appropriate follow up. Psychosocial factors influence antenatal testing and subsequent management, so should be explored at an early stage.

HIV seroconversion is associated with higher viral loads which increases the risk of *in utero* transmission by up to 40%, hence the need for prompt diagnosis, initiation of appropriate antiretrovirals and follow up. Diagnosis of *in utero* transmission can be made by the identification of proviral DNA through amniocentesis or from the cord blood/newborns blood sample at birth, Robust policies should exist in every antenatal unit offering HIV tests, with clear records of uptake and the reasons for declining a test. Reasons for declining should be further explored through a meeting with a dedicated HIV midwife and the obstetrician in charge, with repeat offering of the test. All relevant healthcare staff should have the skills and knowledge to deal with these situations comfortably and receive regular training, peer support and audit in their units.

Methods of MTCT

There are three established ways of MTCT:

- *In utero* transmission is an uncommon mode of transmission as an intact placenta acts as a very effective barrier to the transfer of HIV. Placental transfer of virus can happen with an extremely high viral load which is common in seroconversion illness, advanced late stage disease with very low CD4 and in the presence of opportunistic infections which can upregulate the viral load. The placental barrier can be compromised with severe systemic infections like miliary tuberculosis, falciparum malaria and secondary syphilis where inflammatory endarteritis can distort the integrity of the placenta. Con-comitant use of crack and cocaine can also impair placental function and may increase the risk of MTCT.
- MTCT at the point of delivery is the commonest mode of transmission, and can occur as a result of high viral load at delivery, prolonged rupture of membranes, prematurity, vaginal laceration, vaginal ulceration due to herpes simplex infection or syphilitic ulcers, episiotomy, invasive fetal monitoring and instrumental delivery.
- Postpartum MTCT is almost exclusively due to breast feeding and accounts for up to 40% of transmissions in undiagnosed women. For some women there is a lot of stigma around being unable to breast feed; this can cause great distress, especially in sub Saharan Africa, who see it as a disclosure of their HIV status to friends, families and even partners.

Stigma and mental health conditions in HIV positive pregnant women

Chronic HIV infection, subsequent opportunistic infections, homelessness, stigma, poverty, immigration, disclosure, family and peer pressure and drug use can all contribute to complex mental illness which can affect the engagement of the women with the HIV/Obstetrics team. It can result in late booking and self neglect, and interfere with adherence to ART and follow up. African women, especially from sub Saharan Africa, are the second largest group affected with HIV after men who have sex with men in the UK. About one quarter of HIV positive people in Europe are from Africa (32% in the UK).

Residency status and immigration pose significant problems both in terms of accessing healthcare and right to the care. Undocumented migrants are more likely to be unaware of emergency contraception, to have unintended pregnancy, to present late for their first antenatal visit and to not have an HIV test documented.

The audit on perinatal transmission highlighted that social circumstances aggravated the delivery of optimal care of HIV infected pregnant women and this might have been a contributing factor towards MTCT.

Many HIV positive women are unable to disclose the diagnosis to their partners as they fear violence, separation and rejection. Women may depend on their partners for financial support, right to remain in the UK and accommodation. Disclosure issues are best dealt within a multidisciplinary team approach with the best interests of the women at the centre of discussion. Otherwise, there may be non engagement with