

HKCOG Guidelines

Number 6

Revised
July 2021

Guidelines on the screening, diagnosis and management of HIV in pregnancy

published by The Hong Kong College of Obstetricians and Gynaecologists

A Foundation College of Hong Kong Academy of Medicine



1 INTRODUCTION

The universal antenatal HIV screening programme was implemented in Hong Kong since September 2001. Rapid HIV testing was introduced and integrated into the prevention of mother-to-child transmission (MTCT) programme, targeting women presented late in the peripartum period in 2008. This programme received a high uptake rate; the proportion of women having a known HIV status before labour increased from 91% at 2006 to over 99.9% at 2010 (1).

Over the last decade, the prevalence of HIV infection in Hong Kong remains low, at 0.01%. Likewise, the prevalence of HIV in pregnant women is also low at less than 0.02%, while the perinatal transmission rate has been less than 1% since 2011 (1, 2). The guideline was updated from its first edition in 2001.

2 UNIVERSAL ANTENATAL HIV SCREENING PROGRAMME

Fourth generation enzyme-linked immunosorbent assays are recommended as the first-line test in antenatal HIV screening. (Grade GPP)

A positive screening test must followed by a confirmatory test. (Grade GPP)

High-risk women recommends for HIV retesting in late pregnancy. (Grade GPP)

Women with unknown HIV status present in labour recommends for Rapid HIV test. (Grade GPP)

In Hong Kong, HIV testing usually follows a two-step algorithm, i.e., a screening test followed by a confirmatory test. Enzyme-linked immunosorbent assays (ELISAs) are common approach for HIV screening.

The fourth generation ELISAs detect both HIV antibodies and p24 antigens, and hence, can shorten the window period to two weeks. Although the fourth generation ELISAs have high specificity, false positive results could still occur in pregnancy and among some autoimmune conditions. Therefore, a positive screening test should always followed by a confirmatory test.

HIV confirmatory test could be either Western Blot (WB) or HIV-1/HIV-2 antibody differentiation immunoassay, which detect the presence of HIV antibodies. In the situation where the confirmatory test results are negative after an initial positive screening test result, further virologic testing based on the detection of HIV RNA should be considered.

During the window period of an acute HIV infection, HIV antibodies could remain negative or be indeterminate. In such circumstance, virologic test is useful for

diagnosis. Nevertheless, virologic testing should not be routinely used as an HIV confirmatory test because of possible false negative result in elite controllers (i.e. people with HIV who maintain an undetectable HIV-1 viral load and high CD4 cell counts without the use of antiretroviral therapy). Hence, virologic testing can only be used as a complement

test and should not be used as a standalone test.

Informed consent prior to all HIV testing is recommended due to concerns of psychosocial implications related to HIV infection. In usual circumstances, a verbal consent is sufficient.

Major causes of false-positive and negative HIV ELISA results

False positive

- Antibodies to HLA antigens
- Multiple transfusions
- Recent influenza immunization
- Improper specimen handling e.g. exposed to high temperature

False negative

- Recent infection (at window period)
- Hypogammaglobinaemia
- Advanced HIV infection (a rare cause)
- HIV-2 (limits to those test kits specific for HIV-1)
- Unusual HIV-1 serotype (e.g. Group O)

Rapid test

Rapid test is a qualitative *in vitro* immunoassay for HIV-1 and HIV-2 antibodies. It is recommended for all pregnant women when they present in labour, but without antenatal HIV screening (3). The current generation of rapid test is highly sensitive and specific, so a negative result effectively rules out HIV infection except in acute seroconversion (4). A positive result is highly suggestive of an HIV infection hence prophylactic interventions with Zidovudine (ZDV) against MTCT should be implemented immediately. Nevertheless, confirmation by western blot or other microbiological tests is still required. A rapid test should not be used as a routine test to diagnose HIV infection.

HIV retesting in late pregnancy

It is important to note that a negative HIV test result in early antenatal period does not preclude subsequent HIV infection. There have been five cases of paediatric HIV infection reported in Hong Kong from 2009 to 2015 in which maternal negative result has been obtained during universal antenatal HIV testing programme (6). Both local and international guidelines recommend HIV retesting for individuals at higher risks of HIV acquisition at later stage of pregnancy (6-8).

The followings are examples where HIV re-testing should be offered at 34-36 weeks of gestation:

- Women or sex partners who are intravenous drug user;
- Women who exchange sex for money;
- Women's sex partners with HIV;
- Women who have a new or multiple sex partner during pregnancy;

- Women who have newly acquired sexually-transmitted infections during pregnancy;
- Women who originated from areas of high HIV prevalence e.g. Africa, or whose sex partners did

In case a woman presents with signs and symptoms suggestive of acute HIV infection, HIV re-testing should be done as soon as possible. Health care providers should always reinforce the importance of safe sex to those high-risk women.

3 PRECONCEPTION COUNSELLING

Women with HIV/AIDS at childbearing age should receive appropriate preconception counselling. (Grade GPP)

Women taking dolutegravir based treatment before pregnancy are recommended to take folic acid 5 mg daily because of increased risk in neural tube defect. (Grade C)

Women with HIV/AIDS at childbearing age should receive appropriate counselling on effective contraception to prevent unintended pregnancies. The counselling should include information about the risk of MTCT, effectiveness of interventions and the options of assisted reproduction if they are planning for pregnancies.

Prevention of horizontal transmission should be provided to serodiscordant couples. There is a tendency of higher rate of fetal neural tube defects among women taking dolutegravir (DTG) comparing those taking other types of antiretroviral therapy at conception (2 per 1000 births vs 1 per 1000 births). Folic acid 5mg daily is recommended for women taking DTG who are trying to get pregnant. Screening of other sexually transmitted infections, viral hepatitis and tuberculosis should be offered before conception.

Women should be assessed on the need of hepatitis A and hepatitis B vaccination, especially for those with co-existing hepatitis C infection. Pre-conception vaccination is much preferred, but vaccination after the first trimester is considered safe. The number of doses has to be adjusted if CD4 <300 cells/mm³ due to potentially lower serological response (9). Flu vaccination and acellular pertussis vaccination (dTap) should be offered during pregnancy if there were no other contraindications (10).

4 ANTENATAL MANAGEMENT OF WOMEN WITH KNOWN HIV

Pregnant women who were known to have HIV should be managed by a team experienced in the management of HIV disease in a multidisciplinary team approach, including physicians, obstetricians, paediatricians, nurses and midwives, with the support from social workers and clinical psychologists. (Grade GPP)

Women who require HIV treatment before pregnancy should receive combination antiretroviral therapy (cART) and maintain on lifelong treatment. (Grade A)

Women who are newly diagnosed with HIV infection during antenatal period are recommended to start cART as soon as possible to ensure virologic suppression at delivery. (Grade A)

HIV physician should be involved in the choice of cART and in the monitoring of the response to treatment and subsequent long term follow-up care. (Grade GPP)

Routine dating scan, first trimester combined screening and morphology scan should be performed according to the local hospital guideline. Non-invasive prenatal testing (NIPT) is

recommended for those who were screened high risk. (Grade C)

Screening of other sexually transmitted infections, genital tract infections, viral hepatitis is recommended. (Grade A)

Screening and diagnosis of fetal aneuploidies:

Combined first trimester screening (maternal age, nuchal translucency, beta-human chorionic gonadotrophin, and pregnancy-associated plasma protein A) is the most effective way of screening. If the patient come late, second trimester serum screening test (quadruple test: α -fetoprotein, free β HCG, unconjugated oestriol and Inhibin A) could be offered. However, significantly increased levels of β HCG and α -fetoprotein and lower levels of unconjugated oestriol have been observed in women with HIV causing higher false positive rate (11-13).

Non-invasive prenatal test for trisomy 21, 13, 18 should be offered to women having HIV infection, who are screened high risk in order to reduce the chance of invasive prenatal diagnostic tests (14). However, the use of expanded NIPT is uncertain due to unknown false positive rate of reporting sex chromosome abnormalities and microdeletions. If invasive test is needed, it is considered to be safe if HIV viral load has been adequately suppressed to <50 copies/ml (9).

Although the data are limited to a few case series of less than 100 patients, the risk of perinatal HIV transmission does not appear to increase with the use of invasive diagnostic procedures in women who have virologic suppression on cART (15-18). However, most of the procedures were amniocentesis and a small number of chorionic villous sampling. HIV physicians and maternal fetal medicine subspecialists should be consulted if the woman has a detectable viral load before the procedure.

If the woman is not on cART, but the invasive diagnostic test procedure cannot be delayed until viral suppression is achieved, it is recommended to commence cART including raltegravir (RAL) with a single dose of nevirapine (NVP) 2–4 hours prior to the procedure (9).

Screening of other sexually transmitted infections

Screening of hepatitis B and syphilis are already included in the routine antenatal screening. Other genital tract infections should be screened in early pregnancy and the tests should be repeated at later gestations in women with high-risk behavior. The presence of any other genital infection and its associated consequence of preterm delivery, chorioamnionitis will increase the risk of vertical transmission of HIV, while treatment to gonococcal, chlamydial, and non-specific cervicitis will reduce cervical mucosal shedding of HIV RNA (19).

Screening for viral hepatitis

Pregnant women who were known to have HIV should be screened for both hepatitis B and hepatitis C infection as co-infection is common in HIV-infected individuals due to shared routes of transmission. Moreover, co-infection also affects the choice of drug regimen.

The investigation of newly diagnosed hepatitis B infection should include viral load, e-antigen status, liver ultrasound scan and liver function tests. Liver function tests should be repeated at 2 and 4 weeks after commencing cART to detect potential hepatotoxicity or immune reconstitution inflammatory syndrome. Regular monitoring of liver function throughout pregnancy and postpartum is recommended.

Screening for tuberculosis

The risk of developing tuberculosis (TB) is much greater, and its presentation could be atypical in HIV patients (20). Screening for latent TB infection for HIV infected individuals should be conducted according to the latest recommendation by latest recommendations by the Scientific Committee on AIDS and STI (21).

Use of cART in pregnancy

Current BHIVA treatment guidelines recommend treatment to all HIV infected individuals including elite controller living with HIV regardless of CD4 cell count and the clinical status (9). cART is recommended to all HIV infected women during the antenatal and postpartum period due to the established benefits on their own disease prognosis and for the prevention of MTCT. Women should be counselled about the benefits and potential risks of the medications, as well as the importance of drug adherence.

For women having HIV infection and already engaged in HIV care who become pregnant, evaluation of current antiretroviral therapy should be made regarding antiretroviral potency, potential toxicity to the mother and fetus and prophylactic efficacy against MTCT. The current regimen should be maintained throughout the antenatal period if full viral suppression could be achieved unless there are any major side effects or if the treatment is contraindicated during pregnancy. Women having a detectable viral load despite good compliance should be offered a testing on therapeutic levels of drug and on the possibility of drug resistance (9).

Antiretroviral drugs are classified by the phase of the retrovirus life cycle that the drug inhibits. A typical regimen includes two nucleoside reverse-transcriptase inhibitors (NRTI) as a "backbone" with one protease inhibitor (PI), integrase nuclear strand transfer inhibitors (INSTIs)

or non-Nucleoside reverse-transcriptase inhibitor (NNRTI) as a "base".

Nucleoside reverse-transcriptase inhibitors (NRTIs)

- A combination of two NRTIs as “backbone” is recommended.
- Zidovudine (ZDV) is the only antiretroviral with a license to use in pregnancy. Its combined use with lamivudine (3TC) has been extensively adopted for pregnant patients. However, ZDV is less preferred for the associated risks of reversible maternal and neonatal anaemia and neutropenia. Tenofovir (TDF), Abacavir (ABC) and Emtricitabine (FTC) are also considered safe in pregnancy.
- The choice depends on the side effect profile, frequency of dosing, interactions with the third agent, resistance profile and the presence of co-infection. The pharmacokinetics of most NRTIs are not significantly altered by pregnancy, so dose adjustment is not required for pregnancy.
- The recommended “backbone” combinations are:
 - i. 300 mg ZDV plus 150 mg 3TC (Combivir® twice daily)
 - ii. 300 mg TDF plus 200 mg FTC (Truvada® once daily)
 - iii. 600 mg ABC plus 300mg 3TC (Kivexa® once daily)
- For women who are co-infected with hepatitis B, TDF with either FTC or 3TC is preferred.
- Maternal blood for haemoglobin, glucose and liver enzymes should be monitored to look for anemia, hyperglycaemia and deranged liver function. Deaths from lactic acidosis and liver failure have been associated with the use of two NRTIs, stavudine (d4T) and didanosine (DDL); therefore, combinations involving these drugs should be avoided in pregnancy.

Protease inhibitors (PIs)

- PIs should be given with a pharmacokinetic booster of ritonavir or cobicistat. However, recent pharmacokinetic data suggested that cobicistat-containing antiretroviral regimens should be avoided during pregnancy and postpartum (22). Hence, for women using cobicistat-boosted PI therapy before pregnancy, the boosting agent should be switched to ritonavir in pregnancy, because of its limited placental transfer.
- UK Medicines and Healthcare products Regulatory Agency (MHRA) recently announced that darunavir boosted with cobicistat (DRV/c) should not be initiated and should be avoided during pregnancy (23,24). US Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission also did not recommend the concomitant use of atazanavir and cobicistat (ATV/c) during pregnancy (25).
- Ritonavir-boosted lopinavir (LPV/r, Kaletra®), ritonavir-boosted atazanavir (ATV/r) and ritonavir-boosted darunavir (DRV/r) are the commonly PIs used during pregnancy. There is conflicting data regarding their association with preterm births and other adverse outcomes.
- The decision of which medication to use may also be influenced by the concomitant administration of antacid, H₂ blocker, or proton pump inhibitors. For example, atazanavir/ritonavir (ATV/r) which relies on low pH for absorption can reduce the bioavailability.
- Although the use of once-daily dosing of DRV/r is approved for non-pregnant adults, there are insufficient pharmacokinetic data to support its use in pregnancy. DRV/r needs to be taken twice

daily at 600mg DRV with 100mg RTV. ATV/r is taken once daily at 300mg ATV with 100 mg RTV. Lopinavir (LPV/r) Kaletra® at 200 mg LPV with 50mg RTV should be given twice daily and increased to 500-600mg LPT with 125-150mg RTV twice daily in the third trimester.

- Care should be taken to watch out any potential drug-drug interaction with PI-based regimen and therapeutic drug monitoring should be considered whenever appropriate.

Integrase nuclear strand transfer inhibitors (INSTIs)

- Integrase inhibitors are generally the third drug in the regimen when a PI cannot be used. It is well tolerated during pregnancy and rapidly reduces the viral load. For this reason, they are often used in women who are diagnosed with HIV relatively late in their pregnancy and have high viral load over 100,000 HIV RNA copies/mL.
- RAL is most commonly used; it should be given at 400 mg twice daily as there is limited data on the once daily regimen.
- There has been safety alert for use of its DTG in the pre-conception period and during pregnancy for its potential association of neural tube defects following an observational study from Botswana. However, an updated recommendation from the WHO in 2019 suggests the use of DTG because of its advantages of higher viral suppression and lower potential for drug-to-drug interaction. The risk of neural tube defects has declined since the initial report though it remains statistically significant.
- In December 2019, US Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission also

recommended the DTG as the preferred antiretroviral drug throughout pregnancy, given the advantage of once-daily dosing and being generally well tolerated. The panel strongly recommends that use of DTG be accompanied by appropriate counselling to allow patients and their caring physicians to make joint decisions about treatment (26).

- UK MHRA recently announced that elvitegravir boosted with cobicistat (ELV/c) should not be initiated and should be avoided during pregnancy (23,24).

Non-nucleoside reverse transcriptase inhibitors (NNRTIs)

- NNRTIs have long and often unpredictable half-life. It has low genetic barrier to resistance, and one mutation is sufficient to generate high level drug resistance. Cross resistance between Efavirenz (EFV) and NVP is also common.
- EFV at 600 mg daily is previously considered contraindicated in pregnancy for its teratogenicity observed in monkeys. However, a systematic review of the safety of EFV use in humans during the first trimester found no increase in birth defects among women using the drug (27).
- NVP at 200mg daily increases the risk of serious liver damage in women with CD4 counts greater than 250/ μ l. It is generally avoided in pregnant women. However, given that NVP can cross placenta rapidly, it should be given to untreated women who presented in labour.
- Rilpivirine (RPV) at 25 mg daily is an alternative. Because of its relative lower potency, it should not be used when pre-treatment viral load is higher than 100,000 HIV RNA copies/mL.

Monitoring of viral load and CD4 cell count

Monitoring of plasma viral load (HIV RNA level) and CD4 cell count are necessary to ensure satisfactory control of HIV infection. Viral load and CD4 cell count should be monitored regularly as decided by HIV physician and MFM subspecialists. Viral load should be assessed at 34 to 36 weeks' gestation for the decision on the mode of delivery and the management of the newborn.

Viral resistance

Baseline testing of viral resistance is recommended before the commencement of cART. However, cART therapy should not be delayed till after the viral resistance result available. The therapy should be started as soon as possible since earlier viral suppression has been associated with lower risk of MTCT. The therapy can be modified later based on the resistance results, if necessary. Testing of viral resistance is recommended in case of suboptimal virologic suppression to optimize ART regimen.

Other laboratory tests

Women who are taking cART should undergo OGTT at 24 to 28 weeks' gestation. For women who are receiving protease inhibitor-based regimens before pregnancy, a glucose testing should be arranged in early gestation.

5 INTRAPARTUM MANAGEMENT OF WOMEN WHO WERE KNOWN TO HAVE HIV

Recommended mode of delivery is based on HIV viral load. (Grade C)

Artificial rupture of membranes should be avoided in women with detectable viral loads unless there is a clear obstetric indication. (Grade GPP)

Fetal scalp electrode and fetal blood sampling should be avoided. (Grade GPP)

Mode of delivery

Evidence shows that the MTCT rate is less than 0.5% in women whose plasma HIV RNA <50 copies/mL while receiving cART, irrespective of the mode of delivery (28-30). A planned vaginal delivery is supported in the absence of obstetric complication. Elective caesarean section does not offer additional benefits in the prevention of MTCT.

For women on cART having viral load between 50 to 1000 copies/mL. There is no evidence that elective cesarean section

performed solely for prevention of perinatal transmission has statistically significant benefit. Although some studies showed slightly non-significant increase in perinatal transmissions in vaginal deliveries.

However, UK study showed a 2.4-fold increased risk of transmission for every 1 log 10 unit increase in viral load associated with mode of delivery so elective caesarean section should be offered to mothers with viral load >1000 HIV RNA copies/mL (30, 33). Pre labour caesarean section could be considered taking into account of the actual viral load, the trajectory of the viral load, length of time on antiretroviral therapy, obstetric factors and women’s views as summarized as below:

HIV RNA levels (copies/mL)	Recommended Mode of delivery
< 50	Planned vaginal delivery
50-1000	Elective caesarean section could be considered, taking into account of the actual viral load, the trajectory of the load, length of time on antiretroviral therapy, other obstetric factors, and women’s view
>1000 or unknown	Elective caesarean section

Table 2. Recommendation on the mode of delivery based on HIV viral load.

Timing of delivery

If the delivery is a planned caesarean section, it is recommended to carry out at 38 weeks gestation to decrease the likelihood of onset of labor or rupture of membranes before the delivery. For planned vaginal delivery, the timing of delivery should be the same as HIV-negative women.

Labour or rupture of membranes before elective caesarean sections

It is unclear whether emergency caesarean section carried out after onset of labour or after spontaneous rupture of membranes, can effectively reduce the risk of vertical transmission. Intrapartum anti-retroviral

therapy should be offered while the mode of delivery should then be individualized.

Intrapartum antiretroviral therapy

- HIV RNA levels unknown or > 1000 copies/mL
 - Intravenous ZDV should begin three hours before the elective caesarean section. Women present in labour or with ruptured membranes before the scheduled operation must be individualized at the time of presentation. In that case, intravenous ZDV should be given while the antepartum antiretroviral therapy regimen should be continued.
- HIV RNA levels between 50-1000

copies/mL

- There is inadequate data for whether intravenous ZDV is beneficial for this group of women who are on antepartum cART. Intrapartum intravenous ZDV can be considered, and the antepartum antiretroviral therapy regimen should be continued.
- HIV RNA levels < 50 copies/mL
 - antepartum cART should be continued. Intrapartum intravenous ZDV would not further reduce the risk of MTCT and therefore not required.

Other intrapartum procedures

Artificial rupture of membranes should be avoided in women with detectable viral loads unless there is a clear obstetric indication. Fetal scalp electrode and fetal blood sampling should be avoided. Data for use of fetal scalp electrodes and fetal blood sampling in women who were known to have HIV infection are in the pre-cART era. The evidence about fetal blood sampling and fetal scalp electrode showed conflicting results. Instrumental delivery should only be performed on strict obstetric indications. An experienced obstetrician should decide the choice of instrument, but forceps is preferable as vacuum extraction may be associated with higher rate of fetal scalp injury.

6 POSTPARTUM MANAGEMENT OF WOMEN HAVING HIV INFECTION AND THEIR INFANT

Breastfeeding in general is not recommended. (Grade GPP)

Formulate a contraceptive plan and barrier method as contraception is recommended. (Grade GPP)

Mother

Women should continue cART and medical care under HIV physicians. Breastfeeding in general is not recommended because of the potential risk of MTCT. For women with full viral suppression on cART and good adherence to treatment and choose to breastfeed, the residual risk of HIV transmission through breastfeeding should be fully informed. A plan for contraception postnatally should have been discussed in advance before delivery. Barrier method as contraception is recommended. Drug interaction may happen with co-administration of cART and hormonal contraception. Women who were known to have HIV infection are more likely to have persistent HPV infection, hence annual cervical smear test is advised.

Newborn

All newborns should receive antiretroviral prophylaxis from paediatricians as soon as after birth to minimize the risk of HIV transmission. The type of prophylaxis will depend on the mother's virologic status.

7 SPECIAL CONDITIONS

For pregnant women with HIV infection diagnosed during labour

Intravenous ZDV infusion (at 2mg/kg infused over one hour followed by 1mg/kg/hr) should be administered throughout labour, with or without additional antiretroviral medication e.g. lamivudine or nevirapine if HIV infection is diagnosed only in labour. At postnatal, two-drug antiretroviral regimen should be used to the newborns to reduce the risk of MTCT. HIV physician should be involved in the management and decision on any additional cART.

Screening of other sexually transmitted infections and viral hepatitis should be carried out if these had not been performed antenatally.

In general, caesarean section is the preferred mode of delivery for pregnant women infected with HIV, who had not yet received any cART and whose viral load is unknown. However, the mode of delivery should be individualized and to be discussed with the patient when she is already in active labour with or without rupture of membranes. Women should be referred to HIV physicians for postpartum monitoring, treatment and subsequent long-term care.

Management of preterm delivery and preterm prelabour rupture of membranes (PPROM)

The general obstetric management of preterm delivery and PPRM should not differ in women who were known to have HIV infection. High vaginal swab and mid-stream urine should be taken for culture and sensitivity.

Delivery should be expedited in those with known HIV infection who has PPRM or preterm labour after 34 weeks of gestation. Prophylactic antibiotics covering Group B Streptococcus should be given for women with unknown GBS status. The mode of delivery should follow the recommendations as the session on intrapartum management.

There is no consensus on the optimum management of PPRM and/or preterm labour in those with HIV infection. Decisions regarding the optimum management require multidisciplinary involvement with consideration of the exact gestation, maternal viral load, disease control and the presence of any other co-morbidities.

Antibiotics and antenatal steroids should be given as recommended. Prompt delivery is advised if there is evidence of chorioamnionitis or fetal distress. If maternal and fetal conditions are stable, the decision on timing and mode of

delivery should be made by the obstetrician with consultation and discussion with the neonatologists and HIV physicians based on the holistic assessment.

HIV physicians and neonatologists should be consulted to determine the choice of antiretroviral therapy. Infants born below 32 weeks of gestation may be unable to tolerate oral medications, and thus administering anti-retroviral therapy to the mother just before and during delivery will provide prophylaxis to the neonate, and dosage of antiretroviral drug may have to be adjusted (34).

8 CONCLUSION

The management of HIV in pregnancy should involve a multidisciplinary team with members experienced in managing high risk pregnancy. The use of cART has undergone rapid changes in the recent years so the information in this guideline can only provide the information up till the time of writing. Colleagues should review the latest recommendations by the Scientific Committee on AIDS and STI, British HIV Association and the US Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission on Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States for the most up-to-date recommendation.

9 SUMMARY OF RECOMMENDATIONS

1. Universal antenatal HIV screening programme
 - a. Fourth generation enzyme-linked immunosorbent assays are recommended as the first-line test in antenatal HIV screening.

- b. A confirmatory test by either Western Blot or HIV-1/HIV-2 antibody immunoassay should always be performed after a positive screening test.
 - c. HIV retesting should be offered to high-risk women in late pregnancy.
 - d. Rapid HIV tests should be performed when women with unknown HIV status present in labour.
2. Preconception counselling
 - a. Women with HIV/AIDS at childbearing age should receive appropriate counselling.
 - b. Women taking dolutegravir based treatment before pregnancy are recommended to take 5 mg daily folic acid because of increased risk in neural tube defect.
 3. Antenatal management of women with known HIV
 - a. Pregnant women who were known to have HIV should be managed by a team experienced in the management of HIV disease in a multidisciplinary team approach, including physicians, obstetricians, paediatricians, nurses and midwives, with the support from social workers and clinical psychologists.
 - b. Women who require HIV treatment before pregnancy should receive combination antiretroviral therapy (cART) and maintain on lifelong treatment.
 - c. Women who are newly diagnosed with HIV infection during antenatal period are recommended to commence cART as soon as practicable to ensure virologic suppression at delivery
 - d. HIV physician should be involved in the choice of cART and in the monitoring of the response to treatment and subsequent long term follow-up care.
 - e. Routine dating scan, first trimester combined screening and morphology scan should be performed according to the local hospital guideline. Non-invasive prenatal testing (NIPT) is recommended for those who were screened high risk.
 4. Intrapartum management of women who were known to have HIV
 - a. Artificial rupture of membranes should be avoided in women with detectable viral loads unless there is a clear obstetric indication.
 - b. Fetal scalp electrode and fetal blood sampling should be avoided.
 5. Postpartum management of women having HIV infection and their infant
 - a. Breastfeeding in general is not advised.
 - b. Formulate a contraceptive plan and barrier method as contraception is recommended.
 6. Special conditions
 - a. Caesarean section is the preferred mode of delivery for pregnant women with HIV infection diagnosed during labour.
 - b. Individualized plan should be given if the woman is in active labor

REFERENCE

1. Recommended HIV/AIDS strategies for Hong Kong 2012-2016. Hong Kong Advisory Council on AIDS. 2012.
2. HIV SURVEILLANCE REPORT – 2018 UPDATE, Special Preventive Programme, Centre for Health Protection, Department of Health Hong Kong Special Administrative Region December 2019. Special Preventive Programme, Centre for Health Protection, Department of Health Hong Kong Special Administrative Region December 2019.
3. Scientific Committee on AIDS and STI. Recommended Clinical

- Guidelines on the Prevention of Perinatal HIV Transmission, November 2018.
4. US department of Health and Human Services. Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States. March 2018
 5. Centre for Health Protection. STD/AIDS update: a quarterly surveillance report. Vol 25 No. 1 Quarter 1 2019. Available at <https://www.aids.gov.hk/english/surveillance/stdaidsupdate.html>. Accessed 26 Nov 2020.
 6. Scientific Committee on AIDS and STI: Recommended Clinical Guidelines on the Prevention of Perinatal HIV Transmission. November 2018. Available at https://www.chp.gov.hk/files/pdf/recommended_clinical_guidelines_on_the_prevention_of_perinatal_hiv_transmission_november2018.pdf. Accessed 5 Jul 2019.
 7. Prenatal and perinatal human immunodeficiency virus testing. ACOG Committee Opinion No. 752. American College of Obstetricians and Gynecologists. *Obstetrics & Gynecology* 2018;132:e138–4.
 8. de Ruiter A, Mercey D, Anderson J, Chakraborty R, Clayden P, Foster G, et al. British HIV Association and Children's HIV Association guidelines for the management of HIV infection in pregnant women 2008. *HIV Med* 2008;9(7):452-502.
 9. British HIV Association. British HIV Association guidelines for the management of HIV in pregnancy and postpartum 2018 (2020 third interim update). Available at <https://www.bhiva.org/pregnancy-guidelines>. Accessed 19 Aug 2020
 10. British HIV Association. British HIV Association guidelines on the use of vaccines in HIV-positive adults 2015. Available at <https://www.bhiva.org/file/NriBJHDVKGwzZ/2015-Vaccination-Guidelines.pdf>. Accessed 10 Jan 2021
 11. Gross S, Castillo W, Crane M, Espinosa B, Carter S, DeVeaux R, et al. Maternal serum alpha-fetoprotein and human chorionic gonadotropin levels in women with human immunodeficiency virus. *American Journal of Obstetrics and Gynecology* 2003;188(4):1052-6.
 12. Spencer K. First and second trimester markers of fetal aneuploidy in pregnant women with HIV infection. *Fetal Diagnosis and Therapy* 2011;29(2):135-8.
 13. Yudin MH, Prosen TL, Landers DV. Multiple-marker screening in human immunodeficiency virus-positive pregnant women: screen positivity rates with the triple and quad screens. *American Journal of Obstetrics and Gynecology* 2003;189(4):973-6.
 14. UK National Screening Committee. Screening in the UK: making effective recommendations 2015 to 2016. Available at <https://www.gov.uk/government/publications/uk-national-screening-committee-recommendations-annual-report>. Accessed 19 Aug 2020.
 15. Simões M MC, Gonçalves A, Pereira AP, Correia J, Castela J, et al. Amniocentesis in HIV pregnant women: 16 years of experience. *Infectious diseases in obstetrics and gynecology* 2013;2013:914272.
 16. Ekoukou D K-JM, Ghibaud N, Mechali D, Rotten D. Amniocentesis in pregnant HIV-infected patients. Absence of mother-to-child viral transmission in a series of selected patients. *European journal of obstetrics, gynecology, and reproductive biology* 2017;210:295-9.
 17. Floridia M MG, Meloni A, Cetin I, Tamburrini E, Cavaliere AF, et al. Amniocentesis and chorionic villus sampling in HIV-infected pregnant women: a multicentre case series. *BJOG* 2017;124(8):1218-23.

18. Peters H FK, Harding K, Tookey PA, Thorne C. Operative vaginal delivery and invasive procedures in pregnancy among women living with HIV. *European journal of obstetrics, gynecology, and reproductive biology* 2017;210:295-9.
19. Gitau RW GS, Masese LN et al. Effect of acquisition and treatment of cervical infections on HIV-1 shedding in women on antiretroviral therapy. *AIDS* 2010; 24: 2733–2737.
20. Centers for Disease Control and Prevention. Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: principles of therapy and revised recommendations. *MMWR* 1998;47(No. RR-20)
21. Scientific Committee on AIDS and STI. Recommendations on the Management of Human Immunodeficiency Virus and Tuberculosis Coinfection 2020. Available at https://www.chp.gov.hk/files/pdf/recommendations_on_mgt_of_hiv_tb_coinfection_nov2020.pdf. Accessed 17 Feb 2021.
22. Boyd SD, Sampson MR, Viswanathan P, Struble KA, Arya V, Sherwat AI. Cobicistat-containing antiretroviral regimens are not recommended during pregnancy: viewpoint. *AIDS* 2019;33(6):1089–1093.
23. Medicines and Healthcare products Regulatory Agency. Darunavir boosted with cobicistat: avoid use in pregnancy due to risk of treatment failure and maternal-to-child transmission of HIV-1. Published 17 Jul 2018. Available at <http://www.gov.uk/drug-safety-update/darunavir-boosted-with-cobicistat-avoid-use-in-pregnancy-due-to-risk-of-treatment-failure-and-maternal-to-child-transmission-of-hiv-1>. Accessed 10 Jan 2021
24. Medicines and Healthcare products Regulatory Agency. Elvitegravir boosted with cobicistat: avoid use in pregnancy due to risk of treatment failure and maternal-to-child transmission of HIV-1. Published 16 Apr 2019. Available at <http://www.gov.uk/drug-safety-update/elvitegravir-boosted-with-cobicistat-avoid-use-in-pregnancy-due-to-risk-of-treatment-failure-and-maternal-to-child-transmission-of-hiv-1>. Accessed 10 Jan 2021
25. Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States. [Atazanavir G94 (Last updated December 29, 2020)] Available at <https://clinicalinfo.hiv.gov/sites/default/files/inline-files/PerinatalGL.pdf>. Accessed 9 Jan 2021.
26. Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States. [Appendix D: Dolutegravir Counseling Guide for Health Care (Last updated December 12, 2019)] Available at <https://clinicalinfo.hiv.gov/sites/default/files/inline-files/PerinatalGL.pdf>. Accessed 10 Jan 2021
27. World Health Organisation. A systematic review of the teratogenicity of efavirenz. WHO ART Guidelines meeting review, Oct 2009. Available at https://www.who.int/hiv/topics/treatment/review_teratogenicity_efavirenz.pdf. Accessed 28 Nov 2020.
28. Boer K, Nellen JF, Patel D, Timmermans S, Tempelman C, Wibaut M, et al. The AmRo study: pregnancy outcome in HIV-1-infected

- women under effective highly active antiretroviral therapy and a policy of vaginal delivery. *BJOG*. 2007;114(2):148-55.
29. Warszawski J, Tubiana R, Le Chenadec J, Blanche S, Teglas JP, Dollfus C, et al. Mother-to-child HIV transmission despite antiretroviral therapy in the ANRS French Perinatal Cohort. *AIDS*. 2008;22(2):289-99.
 30. Townsend CL, Cortina-Borja M, Peckham CS, de Ruiter A, Lyall H, Tookey PA. Low rates of mother-to-child transmission of HIV following effective pregnancy interventions in the United Kingdom and Ireland, 2000-2006. *AIDS*. 2008;22(8):973-81.
 31. Boer K, England K, Godfried MH, Thorne C. Mode of delivery in HIV-infected pregnant women and prevention of mother-to-child transmission: changing practices in Western Europe. *HIV Med*. 2010;11(6):368-78.
 32. Mandelbrot L, Tubiana R, Le Chenadec J, Dollfus C, Faye A, Pannier E, et al. No perinatal HIV-1 transmission from women with effective antiretroviral therapy starting before conception. *Clinical Infectious Disease* 2015;61(11):1715-25.
 33. Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States. Intrapartum Care for Women with HIV. D1 (Last updated December 29, 2020) Available at <https://clinicalinfo.hiv.gov/sites/default/files/inline-files/PerinatalGL.pdf>. Accessed 9 Jan 2021.
 34. Desfrere, L. de Oliveira, I. Goffinet, F. El Ayoubi, M. Firtion, G. Bavoux, F. Jarreau, P. H. Moriette, G. Increased incidence of necrotizing enterocolitis in premature infants born to HIV-positive mothers. *AIDS* . 2005 Sep 23;19(14):1487-93.
-
- ACKNOWLEDGEMENT:**
- This document was prepared by Prof WH Tam, Dr YM Wah, Dr Heather KW To, Dr Bonnie CK Wong, Dr LW Law, Dr Teresa WL Ma, Dr Meliza CW Kong and Dr Amelia PW Hui and was endorsed by the Council of the Hong Kong College of Obstetricians and Gynaecologists.
- Special thanks to Dr Heather KW To and Dr Bonnie CK Wong who are the Specialists in Infectious Disease.
-
- This guideline was produced by the Hong Kong College of Obstetricians and Gynaecologists as an educational aid and reference for obstetricians and gynaecologists practicing in Hong Kong. The guideline does not define a standard of care, nor is it intended to dictate an exclusive course of management. It presents recognized clinical methods and techniques for consideration by practitioners for incorporation into their practice. It is acknowledged that clinical management may vary and must always be responsive to the need of individual patients, resources, and limitations unique to the institution or type of practice. Particular attention is drawn to areas of clinical uncertainty where further research may be indicated.
- First version published November 2001