HIV TESTING IN THE NEONATAL PERIOD

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• Evolving PMTCT interventions & 6-week HIV PCR testing

• The diagnostic performance of HIV PCR at birth

• When should neonates have an HIV PCR test?

• Optimal response to a neonatal HIV PCR result that is:

  • positive
  • negative
  • indeterminate
Evolving PMTCT interventions and 6-week HIV PCR testing

2000

Serial HIV ELISA tests to 18 months of age in HIV-exposed infants

2004

Single HIV DNA PCR test at 6 weeks of age to detect virtually all perinatal (in utero & intrapartum) infections (Sherman et al. PIDJ 2005)

sd NVP at birth
① High HIV-related mortality that occurs prior to testing at 6 weeks of age

CHER study – initiate cART at ± 7 weeks of age to reduce morbidity and mortality

(Violari, NEJM, 2008)

±20% mortality in perinatal HIV-infected infants by 13 weeks of age

(Marston, Int J Epidemiol, 2011)

±20% of IU-infected infants LTFU or die by 6 weeks

(Lilian PIDJ 2012)
Effect of maternal and infant PMTCT prophylaxis on sensitivity of HIV PCR test

2010 SA PMTCT guidelines

Simultaneous introduction of

- daily dose NVP for 6 weeks to infant
- HIV TNA PCR test replaced HIV DNA PCR

HIV TNA PCR on same day as final dose of NVP, a potent viral load lowering drug
ARV & HIV PCR (In)Sensitivity

- In in utero infected infants, sdNVP reduced infant VL to below the limit of detection in 38% at 5 days of age and 17% at 2 weeks of age (Mphatswe AIDS 2007, Lilian JCM 2012)

- the probability of a positive HIV PCR at age 6 weeks in perinatally HIV-infected infants is decreased with multi-drug maternal and/or infant PMTCT prophylaxis (Shapiro IAS, 2011)

- in formula fed infants who received 6 weeks of postpartum AZT, with or without other antiretrovirals, 32% of IP-infected infants tested HIV DNA PCR negative at 6-weeks of age but positive at 3 months of age (Nielsen-Saines NEJM 2012)

- Case studies (Haeri Mazenderani SAMJ 2014, Connolly PIDJ 2013)
6 week PCR is too ..... 

- .... LATE to reduce early morbidity & mortality

- .... EARLY to identify all perinatal HIV infections
HIV PCR at birth

- Birth HIV PCR sensitivity for perinatal HIV infection <100%
- Prior to PMTCT or standardized HIV PCR tests - 38% of all perinatal HIV infections detectable at birth (Dunn 1995)
- WHO Option A & sdNVP to infant – 76% of all perinatal infections detectable at birth (Lilian PIDJ 2012)

Birth testing:
- majority women in SA deliver in facilities in SA therefore ± ¾ of all perinatal infections detectable with ±100% coverage
- no routine neonatal visits at delivery facility for HIV PCR result to be returned to neonate
- intrapartum infections undetected unless additional HIV PCR test performed
In utero | Intrapartum | Postnatal

100 HIV+
70
30

70 HIV+
6 wk PCR
20
50
20
10

70 HIV+
Birth PCR
70
30
When should neonates have an HIV PCR test?

- In SA, no diagnosis of neonatal HIV infection because no HIV PCR test recommended (unless symptomatic)
- No accurate national data for HIV-related neonatal mortality
- Modeling the optimal timing of HIV PCR testing in South Africa considering birth, 6-, 10- & 14-week EPI visits
  - 1 HIV PCR test – identifies the same number of HIV+ infants at birth as at 6-weeks
  - 2 HIV PCR tests – most HIV+ infants identified at birth and 10-weeks of age (Lilian JAIDS in press)
When should neonates have an HIV PCR test?

**Targeted birth testing** for neonates at high risk of infection e.g.

- Neonate premature or LBW
- Mother diagnosed at delivery or detectable VL

**Universal birth testing** – test all HIV-exposed neonates

Evaluate:

- Evidence for ‘high risk factors’
- Cost of universal birth PCR test vs ease of implementation
- Implications for public health system of changing guidelines
Optimal response: POSITIVE birth HIV PCR result

- urgent call back – communication with labs & follow up to link all HIV PCR+ to care,
- confirmation of diagnosis with 2nd virological assay
- initiate cART

Don’t delay cART for confirmatory assay but obtain confirmatory results ASAP because progressively more difficult on ARVs to detect HIV either on VL or HIV PCR
Optimal response: NEGATIVE birth HIV PCR result

- Birth test negative, ideally repeat test at 10 weeks
- SA National guidelines recommend 6 weeks
- US guidelines recommend virological assay 2-4 weeks after combination ARV infant prophylaxis has discontinued if HIV PCR negative during prophylaxis

- As for all HIV-exposed and –uninfected infants, HIV PCR is recommended
  - Clinical features suggestive of HIV infection
  - 6 weeks post weaning of breastmilk (unless >18months of age at test – HRT/ELISA)
Optimal response: INDETERMINATE birth HIV PCR result

- Increase in indeterminate HIV PCR test results – creates confusion and reduced efficiency in field
- Occur at 6 weeks and birth
- ??????????
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Ideal Algorithm?

PCR

6 week PCR

PCR

6 weeks post cessation of breastfeeding

18 month rapid test

PCR

Birth PCR

10 week PCR

PCR

Post cessation of breastfeeding

9 month rapid test

PCR (20%)

18 month rapid test

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