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Our Issues, Our Drugs, Our Patients

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Tuberculosis and pregnancy

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Consequences of TB in pregnancy

- Low birth weight
- Prematurity
- Congenital TB
- Increased neonatal and maternal mortality
- Increased pregnancy complications
- Abortion
- Post partum haemorrhage
- Pre-eclampsia
Consequences of TB in pregnancy

Pregnant women with pulmonary TB who access early appropriate TB treatment do not have an increase in maternal or neonatal complications.
Incidence of TB in pregnancy
• Therefore it is important to:
  Prevent TB in pregnancy
  Diagnose and treat TB in pregnancy
Prevention

Improve immunity among HIV infected people

Expansion of ART is associated in a reduction in TB associated maternal mortality

Treat latent TB
Treating latent TB – non pregnant populations

• Absence of HIV, INH has a 62% reduction in TB in people with a positive TST (Smieja MJ et al 2000, Cochrane database)

• South African adult HIV positive largely on ART. RCT of 1635. INH+ ART reduced incidence of TB > ART alone. TST not important. No difference in mortality. (Rangaka MX et al 2015, Lancet)
Treating latent TB – non pregnant populations

• SA paediatric population; advanced HIV with no ART 263 children randomised to INH/placebo. Study stopped survival benefits in IPT compared to control arm (72% reduction) (Zar H et al, 2007 BMJ)

• SA paediatric population; HIV positive, ART and HIV exposed, RCT IPT compared to a control group. No difference in outcomes. (Madi S et al, 2011 NEJM)
Lessons learned from non-pregnant populations

• Need information on the population of interest, extrapolation may not be accurate

• Effective screening reduces the ‘incidence’ of TB more effectively than INH prophylaxis

• INH does not reduce mortality
Prevention

Limited data in pregnancy (3 studies – 2 in US)

Higher risk of INH hepatitis in pregnant than non pregnant women – although this was not significant.

Low adherence to INH therapy in all three studies

Nguyen HT et al. 2014 BMC Infect Dis

LTB treatment in pregnancy, 2000. MMWR
Prevention INH prophylaxis in pregnancy

ART more beneficial overall than INH

Added/common toxicity between ART, INH and pregnancy

Risk benefit is different in pregnancy than general population
Prevention

• Screen women effectively
• Initiate ART and stabilise women on treatment
• Wait until post partum period unless high risk – for TB such as household exposure
• Research in pregnant women
• DoH advocates INH for all HIV positive pregnant women
Diagnosis

• Studies have shown delays in diagnosis
• Clinical symptoms overlap with pregnancy symptoms
• Need a low threshold to send specimens
Treatment of TB in pregnancy

- Fourteen studies have been conducted with treatment outcomes, including 375 pregnant women treated for TB
- Good treatment outcomes with 88.5% cure rate.
- The mortality was 6.6% - most due to meningitis or MDR TB
Treatment of TB in pregnancy

- Streptomycin was not used in a single pregnant women among these studies.
- All other first line agents can be used (INH, Rif, ETB, PZA) and appear not to be associated with congenital abnormalities.
- Remember pyridoxine (50mg daily) supplementation.
- No dose adjustments in pregnancy required.

Loto OM et al. 2012 Journal of pregnancy
Denti P et al. 2015. AAC
Treatment of MDR TB in pregnancy

- 55 pregnant women with MDR were treated
  - 11 women died
  - 6 women opted for TOP
  - 1 still birth
  - 1 early infant death d/t pneumonia
  - 1 loss to follow up
- The remaining women were successfully treated
- MDR TB in pregnancy can be cured

Nguyen HT et al. 2014 BMC Infect Dis
Treatment of MDR TB in pregnancy

- Kanamycin, Amikacin, Capreomycin and fluoroquinolones are all CI in pregnancy
- However, they should be used with MDR TB in pregnancy as per sensitivity profile
- Pregnant women with MDR TB have been treated with: aminoglycosides, fluoroquinolones, thiomides, cycleserines and terizidone

TB elimination, 2012, CDC
Loto OM et al. 2012 Journal of pregnancy
Treatment of MDR TB in pregnancy

- Curing TB is the more important objective
- Where a number of treatment options exist: Fluoroquinolones seem to be ok
- Avoid aminoglycosides (if needed amikacin is preferred to streptomycin)
- Replace prothinomide and ethionamide (toxic in animal studies) with PAS
- Reduce fetal levels of capreomycin by only using it 3 times a week
Conclusion

Important to diagnose and treat TB in pregnancy early to ensure favourable outcomes

TB is difficult to diagnose in pregnancy

Treat primary TB as per non pregnant women

Tailor treatment in MDR TB where possible

Benefit:risk of treating latent TB in pregnancy still needs to be determined