Policy 4.3  Tuberculosis (active and latent) in Pregnancy

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Related WA TB Control Program Policies

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1.2 Diagnosis of tuberculosis – Clinical
2.1 Medical treatment of tuberculosis (adults)
2.2 Case management of tuberculosis
3.1 Diagnosis of latent tuberculosis infection
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9.1 Management of confidential information for the WA Tuberculosis Control Program
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9.3 Fees and charges associated with tuberculosis and leprosy treatment

Document Control

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1.0 Introduction

Active tuberculosis (TB) in pregnant women not only has adverse consequences on the mother and her pregnancy, but can also lead to infection in the neonate during the antenatal, intrapartum and post partum periods. The neonate can acquire infection through haematogenous spread via the placenta and umbilical vessels, aspiration or ingestion of infected amniotic fluid or maternal genital secretions or by air borne transmission from an infected mother in the post natal period (Adhikari & Jeena, 2009). Most cases of neonatal TB are due to airborne spread after delivery. Breast milk does not transmit TB. Transmission of TB from mother to baby is more likely to occur if the mother has miliary or untreated TB, microscopy detectable acid fast bacilli in sputum specimens or when maternal disease is diagnosed late (Adhikari & Jeena, 2009).

If left untreated, TB in pregnancy can have a mortality rate of 30-40%, and pregnancy related complications are seen more frequently (Adhikari & Jeena, 2009). Maternal complications include a higher frequency of miscarriage, pre-eclampsia and pre-term labour (Ormerod, 2001). Effects on the foetus include higher rates of perinatal mortality, prematurity and poor foetal growth. The risk of complications is increased with late diagnosis.

2.0 Active Tuberculosis in Pregnancy

The clinical presentation of tuberculosis (TB) in pregnancy is similar to that in non-pregnant women but diagnosis may be delayed by non-specific symptoms of malaise and fatigue, which also occurs in pregnancy (Ormerod, 2001). Any delay in diagnosis and treatment increases the risk of obstetric and perinatal complications. Diagnosis may also be late when chest x-ray is postponed or delayed due to concerns of radiation exposure to the developing foetus. Extrapulmonary TB occurs in 5-10% of TB diagnosed in pregnant woman, which is comparable with non-pregnant women (Adhikari & Jeena 2009; Ormerod, 2001).

The clinical assessment and investigations used to investigate suspected tuberculosis in pregnant women are the same as the general population (see the WA TB Control Program polices 1.1 and 1.2 Diagnosis of Tuberculosis). Investigations should include the examination and culture of sputum specimens for M.tuberculosis and other specimens collected as appropriate for those body sites involved e.g. lymph node aspirate, pleural fluid, and endometrial samples. The placenta delivered from a mother with TB, especially if disseminated or miliary, should be examined microbiologically and histologically for evidence of TB. A chest x-ray is required if recent infection is suspected to look for asymptomatic but radiological active pulmonary TB and can be performed with abdominal lead shielding to protect the foetus.
2.1 Medical Treatment

If TB is diagnosed in a pregnant woman, treatment must be started as soon as possible to avoid the serious effects of tuberculosis upon the women, upon the foetus and the neonate, and to limit the infectiousness of the woman.

First-line treatment of TB in pregnant women is no different to non-pregnant women. The standard 6-month regimen of an initial 2 months isoniazid, rifampicin, ethambutol and pyrazinamide followed by 4 months of isoniazid and rifampicin (2HREZ4HR) is used with daily dosing rather than intermittent therapy preferred. For details of drug doses and circumstances in which this regimen may be altered see the WA TB Control Program policy 2.1 Medical Treatment of Tuberculosis (adults) sections 5.0 and 6.0.

Pyrazinamide

In some jurisdictions (American Thoracic Society, CDC and Infectious Diseases Society of America, 2003) pyrazinamide is not recommended for routine treatment of TB in pregnancy, because of a lack of published evidence regarding its safety. Conversely the WHO (World Health Organisation, 2009) and the International Union Against TB & Lung Disease (Caminero, 2003) do not recommend against its use, and it has an Australian Category B2 classification for risk of drug use in pregnancy. Given the lack of reported adverse outcomes in pregnancy and the importance of PZA in short course chemotherapy of TB, pyrazinamide is recommended for routine use in pregnant patients in WA (Therapeutec Guidelines Limited, 2010). This discrepancy in recommendation should be discussed with the patient at the beginning of therapy and in gaining the patient's informed consent to use an unlicensed product.

If pyrazinamide is not included in treatment, a nine month regimen should be used consisting of an initial 2 months of isoniazid, rifampicin and ethambutol therapy followed by a 7 month continuation phase of isoniazid and rifampicin (2HRE7HR) (American Thoracic Society, CDC and Infectious Diseases Society of America, 2003).

Rifampicin

Bleeding attributable to hypoprothrombinaemia has been reported in newborn infants and in mothers after the use of rifampicin during late pregnancy. This is a rare adverse outcome. The physician treating the TB should ensure the midwife and/or obstetrician managing the delivery is aware of this possibility. MIMS©¹ recommends the mother and newborn receive Vitamin K (MIMS, 2012), but there is no evidence to support this, and in WA it is not routine management. This is not a reason to stop or withhold treatment with rifampicin.

¹ MIMS© is an Australian comprehensive medicines reference.
The following drugs are contraindicated in pregnancy (Ormerod, 2001):

- Aminoglycosides, including Kanamycin and amikacin
- Streptomycin (ototoxic to the foetus),
- Ethionamide (CNS defects) and
- Capreomycin (use with caution if absolutely required)

Liver function should be monitored frequently due to the increased risk of drug-associated liver toxicity during pregnancy and the early peripartum period.

**Pyridoxine**

Pyridoxine supplementation is recommended for all pregnant or breastfeeding women taking isoniazid (World Health Organisation, 2009). Isoniazid-induced peripheral neuropathy usually presents as numbness or a tingling or burning sensation of the hands or feet and occurs more commonly in pregnant women. The dose of pyridoxine should be 25mg / day (Centers for Disease Control and Prevention, 2008).

Babies being breastfed by mothers who are taking isoniazid should be given pyridoxine 5 mg daily on the days that the mother receives her isoniazid dose (Therapeutic Guidelines Limited, 2010).

### 2.2 Labour

Those women with fully susceptible pulmonary TB on first-line treatment should not be infectious after two weeks of commencement of anti-TB therapy and should be allowed to deliver as normal. If delivery occurs prior to two weeks of anti-TB therapy and the mother has sputum smear positive TB, then delivery should be conducted in a negative pressure room and appropriate infection control measure taken. The neonate will require preventive treatment and contact tracing procedures followed as usual.

### 2.3 Breastfeeding

Breast-feeding should not be discouraged if a woman is on treatment for active TB. The concentration of anti TB medication found in breast milk is not associated with toxicity to the neonate and all breastfeeding mothers who are receiving isoniazid medication should continue to take pyridoxine supplement (World Health Organisation, 2009, Centers for Disease Control and Prevention, 2008). The concentration of anti-TB medication found in breast milk is too small to be an effective treatment for TB or latent TB in the nursed baby. The neonate born to mothers with active TB should receive their own treatment for either active TB or preventive therapy, with pyridoxine supplement as discussed below.
3.0 Perinatal tuberculosis

Transmission of TB from a mother to the foetus or neonate is most likely to occur when the mother has untreated or disseminated TB, sputum smear positive TB or when TB is diagnosed late in the pregnancy. Perinatal tuberculosis encompasses tuberculosis acquired by the baby while i) in-utero, ii) intrapartum and iii) in the postnatal period.

Tuberculosis acquired by the foetus in-utero from haematogenous spread via the umbilical cord, or in-utero aspiration or ingestion of infected amniotic fluid is rare. It should be considered if the mother has been diagnosed with genital tract TB, especially if late in the pregnancy, and the neonate develops signs of sepsis.

Tuberculosis can be spread to the neonate during delivery by aspiration or ingestion of infected amniotic fluid or cervicovaginal secretions. Tuberculosis infection acquired after delivery occurs from airborne infection from the mother, an adult family carer or another infectious adult with whom the infant has had contact (including health care workers).

3.1 Medical management

A paediatric specialist should always be involved in the management of children at risk of or suspected to have neonatal tuberculosis. The diagnosis of perinatal tuberculosis is difficult and frequently delayed. If the neonate exhibits any signs or symptoms of TB infection then a thorough assessment and investigation should be undertaken for bacterial confirmation of M. tuberculosis infection. Symptoms and signs that should raise suspicion of TB in a neonate born to a mother diagnosed with active TB would be fever, respiratory distress, hepatosplenomegaly, jaundice, lymphadenopathy or an abnormal chest x-ray. The clinical features can be subtle and difficult to differentiate from other congenital / neonatal infections.

Standard anti-TB therapy should be commenced after appropriate specimens have been collected. Paediatric drug regimens and doses are discussed in more detail in the WA TB Control Program policy 4.1 Tuberculosis (active and latent) in children.

After active TB has been excluded in the baby, the neonate should receive preventive therapy as per normal contact tracing procedures. Infants who have been exposed to a mother with fully susceptible TB should be offered preventive therapy with either 6 months isoniazid (10mg/kg) and pyridoxine supplement (5-10 mg daily), or 3 months combination therapy of isoniazid (10mg/kg) and rifampicin (15mg/kg) with pyridoxine supplement (World Health Organisation, 2010). During treatment dosages may require adjustment to reconcile the effect of age, weight gain and possible toxicity in young infants. The decision to adjust dosages should be taken by a clinician experienced in managing paediatric tuberculosis.

If during the period of preventive therapy the infants develops clinical symptoms or signs or radiological appearances suggestive of active TB then appropriate investigations should be done to exclude active TB and a complete course of anti-TB treatment considered.
Contact tracing among the rest of the family and other close contacts of the infected mother must also be performed. This is to ensure that others are not infected with TB.

4.0 Latent Tuberculosis in Pregnancy

4.1 Screening

Routine screening for latent TB infection (LTBI) in pregnancy is not necessary, however, it may be warranted in selected groups:

- Close contacts of infectious TB.
- Recent arrivals from countries with TB incidence rate of >50 per 100,000 population. Individual country incidence rates for TB can be found through the World Health Organisation tuberculosis country profile website [http://www.who.int/tb/country/data/profiles/en/index.html](http://www.who.int/tb/country/data/profiles/en/index.html).
- HIV infected patients (and other profoundly immunocompromised patients).

The tuberculin skin test (TST) is the test of choice and tuberculin reactivity is not affected by pregnancy. It is considered both a valid and safe test to use in pregnancy. The Interferon Gamma Release Immunoassays (IGRAs), of which QuantiFERON-TB Gold In-Tube (QIFN) test is used in Western Australia, are also safe to use in pregnancy for screening, but this test has not been validated for pregnant women.

It is recommended that asymptomatic pregnant women with a positive TST or QIFN and with risk of progressing to active disease e.g. recent contact of TB, HIV co-infection, should have a chest x-ray after 12 weeks gestation to exclude asymptomatic but radiological active pulmonary TB. However, if the patient is not agreeable to this, then it can be deferred until after pregnancy.

4.2 Treatment

The preferred regimen for preventive therapy in pregnant women is isoniazid daily for 6 months with pyridoxine 25mg/day supplementation. Isoniazid is a category A drug and is safe to use in pregnancy. The usual dose is 300mg per day. The decision to treat should be made in conjunction with the patient’s preference. Treatment should be encouraged during pregnancy when there is a high risk of progression to active disease. That is if the woman:

- Is a recent close contact with active TB,
- Has HIV infection or is severely immunocompromised, or
- Has another medical condition, which increases the risk of reactivation of LTBI.

If preventive treatment is to be deferred until after delivery then the pregnant woman should be closely monitored for signs of active disease.
5.0 Conclusion

*M.tuberculosis* infection in a pregnant woman can not only cause disease in the mother, but also expose the foetus and neonate to an increased risk of TB. A high index of suspicion for TB should be present when assessing a woman from a high TB prevalent country or who is a recent contact of TB especially if she exhibits any symptoms or signs of active TB disease. Any delay is diagnosis or investigation for TB should be avoided. First-line treatment for TB is the same in pregnant women as for non-pregnant women and pyridoxine supplement should always be given. Post delivery the neonate must be assessed for active TB disease and appropriate treatment commenced in consultation with a paediatrician experienced in TB management. If active disease in the neonate is absent then preventive therapy should be offered. Breast-feeding should still be encouraged in TB affected mothers.

6.0 Works Cited


**Endorsing Authority**

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**References (Standards)**

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**Feedback or comments related to this policy should be addressed to the Medical Director, WA TB Control Program Justin.Waring@health.wa.gov.au**