



**Thyroglobulin antibodies impair fertility and litter parameters and impact fetal survival in a rodent model of Autoimmune Thyroiditis**

Rebecca L Brady, Nykola L Kent, Anna Reid, Dayna A Zimmerman, James SM Cuffe

*School of Biomedical Sciences, the University of Queensland*

**Background:** Autoimmune thyroiditis (AIT), also known as Hashimoto's disease, is one of the most common causes of thyroid disease and is characterised by auto-antibodies targeting various proteins of the thyroid gland. AIT is associated with infertility and reproductive complications, and 1 in 5 women have elevated thyroid autoantibodies during pregnancy. AIT is associated with increased risk of many pregnancy complications, including gestational diabetes mellitus and fetal growth restriction. These complications present in women who are euthyroid and who have subtle thyroid dysfunction. Despite the overwhelming evidence for an association between AIT and pregnancy complications, there is limited research looking into the underlying mechanisms. Therefore, this study aimed to establish an animal model of AIT during pregnancy to investigate the impact of thyroid antibodies on physiological systems.

**Methods:** Female Lewis rats were either given five subcutaneous injections of porcine thyroglobulin (2ng/ml) and Freund's adjuvant (AIT, n=10) or saline (control, n=10) over the course of seven weeks prior to mating. AIT rats were given access to drinking water with excess sodium iodide (5% w/v) throughout the study. Estrous cycle was monitored using a vaginal electrical impedance monitor and animals were mated when they reached the peak of impedance indicating the proestrus stage. Plasma was collected 1 week prior to mating and at the end of pregnancy to assess plasma thyroid antibody and hormone levels using ELISA. All rats were culled at E20, and tissue collected for further analysis.

**Results:** AIT rats gained less weight prior to pregnancy and had disrupted estrous cycling compared to controls. Plasma concentrations of thyroglobulin antibodies were increased in AIT rats compared to controls both prior to pregnancy and at late gestation. TSH levels were unchanged, and thyroxine was elevated in late gestation. Fetuses from AIT dams also had increased plasma concentrations of thyroglobulin antibodies. AIT did not impact litter size but did cause reduced male fetus survival.

**Conclusions:** These findings demonstrate that even a modest elevation in thyroglobulin antibodies can lead to changes in both fertility and pregnancy outcomes. As there is currently no treatment for AIT, understanding the relationship between AIT and pregnancy complications is essential to maximise the health of maternal and fetal systems. This study highlights the complex presentation of AIT in pregnancy and provides a solid basis for future research to build upon.