

## Association between thyroid autoantibodies and miscarriage and preterm birth meta-analysis of evidence.

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### Abstract

**OBJECTIVES:** To evaluate the association between thyroid autoantibodies and miscarriage and preterm birth in women with normal thyroid function. To assess the effect of treatment with levothyroxine on pregnancy outcomes in this group of women.

**DESIGN:** Systematic review and meta-analysis.

**DATA SOURCES:** Medline, Embase, Cochrane Library, and SCISEARCH (inception-2011) without any language restrictions. We used a combination of key words to generate two subsets of citations, one indexing thyroid autoantibodies and the other indexing the outcomes of miscarriage and preterm birth.

**STUDY SELECTION:** Studies that evaluated the association between thyroid autoantibodies and pregnancy outcomes were selected in a two stage process. Two reviewers selected studies that met the predefined and explicit criteria regarding population, tests, and outcomes.

**DATA SYNTHESIS:** Odds ratios from individual studies were pooled separately for cohort and case-control studies using the random effects model.

**RESULTS:** 30 articles with 31 studies (19 cohort and 12 case-control) involving 12,126 women assessed the association between thyroid autoantibodies and miscarriage. Five studies with 12,566 women evaluated the association with preterm birth. Of the 31 studies evaluating miscarriage, 28 showed a positive association between thyroid autoantibodies and miscarriage. Meta-analysis of the cohort studies showed more than tripling in the odds of miscarriage with the presence of thyroid autoantibodies (odds ratio 3.90, 95% confidence interval 2.48 to 6.12;  $P < 0.001$ ). For case-control studies the odds ratio for miscarriage was 1.80, 1.25 to 2.60;  $P = 0.002$ ). There was a significant doubling in the odds of preterm birth with the presence of thyroid autoantibodies (2.07, 1.17 to 3.68;  $P = 0.01$ ). Two randomised studies evaluated the treatment with levothyroxine on miscarriage. Both showed a fall in miscarriage rates, and meta-analysis showed a significant 52% relative risk reduction in miscarriages with levothyroxine (relative risk 0.48, 0.25 to 0.92;  $P=0.03$ ). One study reported on the effect of levothyroxine on the rate of preterm birth, and noted a 69% relative risk reduction (0.11 to 0.90).

**CONCLUSION:** The presence of maternal thyroid autoantibodies is strongly associated with miscarriage and preterm delivery. There is evidence that treatment with levothyroxine can attenuate the risks.