

INPLASY PROTOCOL

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None declared.

Risk of Adverse Pregnancy Outcomes in Young Women with Thyroid Cancer: Systemic Review and Meta-Analysis

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Review question / Objective: We aim to investigate whether patients with thyroid cancer who underwent thyroidectomy with or without RAIT had increased adverse pregnancy outcomes, including miscarriage, preterm delivery, and congenital malformations through a meticulous meta-analysis and systematic review.

Condition being studied: Thyroidectomy and radioactive iodine treatment (RAIT) are standard treatments for differentiated thyroid cancer (DTC). All patients who undergo total thyroidectomy and more than half of the patients who receive less-than-total thyroidectomy receive thyroid hormone replacement after thyroidectomy, and some of them require thyroid hormone suppression therapy. Therefore, the adverse effects of over- or under-replacement of thyroid hormone after thyroidectomy can last lifelong. Particularly in pregnant women, the importance of adequate thyroid hormonal status has been emphasized in association with pregnancy outcomes. RAIT has been administered in 45–55% of all patients with DTC and several adverse events have been reported, including temporary amenorrhea/oligomenorrhea, earlier onset of menopause, infertility, or adverse pregnancy outcomes. A recent meta-analysis involving four studies reported that RAIT was not associated with decreased birthrate, although there was significant heterogeneity among the included studies. Considering the progressively increasing incidence of DTC in younger women, the association of thyroid cancer treatment with adverse pregnancy outcomes, as well as infertility, can be one of the important issues for women with DTC. Although several case-control studies and case series attempted to investigate the association, evidence regarding adverse pregnancy outcomes in patients with DTC is still inconclusive.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 April 2022 and was last updated on 13 April 2022 (registration number INPLASY202240075).

INTRODUCTION

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cancer who underwent thyroidectomy with or without RAIT had increased adverse pregnancy outcomes, including miscarriage, preterm delivery, and

congenital malformations through a meticulous meta-analysis and systematic review.

Condition being studied: Thyroidectomy and radioactive iodine treatment (RAIT) are standard treatments for differentiated thyroid cancer (DTC). All patients who undergo total thyroidectomy and more than half of the patients who receive less-than-total thyroidectomy receive thyroid hormone replacement after thyroidectomy, and some of them require thyroid hormone suppression therapy. Therefore, the adverse effects of over- or under-replacement of thyroid hormone after thyroidectomy can last lifelong. Particularly in pregnant women, the importance of adequate thyroid hormonal status has been emphasized in association with pregnancy outcomes. RAIT has been administered in 45–55% of all patients with DTC and several adverse events have been reported, including temporary amenorrhea/oligomenorrhea, earlier onset of menopause, infertility, or adverse pregnancy outcomes. A recent meta-analysis involving four studies reported that RAIT was not associated with decreased birthrate, although there was significant heterogeneity among the included studies. Considering the progressively increasing incidence of DTC in younger women, the association of thyroid cancer treatment with adverse pregnancy outcomes, as well as infertility, can be one of the important issues for women with DTC. Although several case-control studies and case series attempted to investigate the association, evidence regarding adverse pregnancy outcomes in patients with DTC is still inconclusive.

METHODS

Participant or population: Pregnant women aged 20 years or older.

Intervention: Total thyroidectomy with/without RAIT or subtotal thyroidectomy.

Comparator: Pregnant women without thyroid cancer.

Study designs to be included: Case-control or case series designs using a registry of patients with thyroid cancer.

Eligibility criteria: (1) population: pregnant women aged 20 years or older; (2) intervention: total thyroidectomy with/without RAIT or subtotal thyroidectomy; (3) comparators: pregnant women without thyroid cancer in case-control studies. There are no comparators in the case series studies; (4) outcomes: miscarriages (abortions), preterm deliveries, and congenital malformations; and (5) study design: case-control or case series designs using a registry of patients with thyroid cancer.

Information sources: Two investigators will search citation databases, including PubMed and EMBASE, and extracted data independently using the predefined tables for data extraction.

Main outcome(s): The event rates and odds ratios of adverse pregnant outcomes including miscarriages, preterm labors and congenital malformation.

Quality assessment / Risk of bias analysis: We will use the Newcastle-Ottawa Quality Assessment Scale to assess the methodological quality of the case-control study

Strategy of data synthesis: The pooled prevalence of adverse pregnancy outcomes will be calculated using the event rates from each study. The odds ratio (OR) and 95% confidence interval (CI) of each study will be computed using the Mantel–Haenszel method. Heterogeneity among the studies will be tested using Higgins I^2 statistic, where an $I^2 \geq 50\%$ indicated heterogeneity. We will compute the ORs using a random-effects model. The publication bias will be tested using the Egger test and a funnel plot. All statistical analyses and graphical presentations will be conducted using the Comprehensive Meta-Analysis software version 3 (Biostat, Englewood, NJ, USA).

Subgroup analysis: We will conduct subgroup analysis according to the radioactive iodine ablation treatment (RAIT) because RAIT in patients with thyroid cancer is important issue for pregnant outcome Intervention type : thyroid cancer without RAIT/with RAIT Planned analytic approach: The odds ratio using the Mantel-Haenszel method.

Sensitivity analysis: We will conduct sensitivity analysis by omitting each study from pooled analysis.

Country(ies) involved: South Korea.

Keywords: thyroid cancer; radioactive iodine treatment; pregnancy outcomes; adverse effects.

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