INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Bacterial and viral infection-related risk of autoimmune thyroid disease: Meta-analysis of cohort and case–control studies

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Review question / Objective: **This meta-analysis estimated the association between Bacterial and viral infections and AITD risk**
Condition being studied: **Autoimmune thyroid diseases (AITDs) are organ-specific autoimmune diseases caused by disorders of autoimmune mechanisms. There are more women than men, and the ratio of women to men is 5~10:1. Including Graves disease (GD), Graves eye disease (GO), Hashimoto's thyroiditis (HT) and postpartum thyroiditis (PPT), etc., which are characterized by thyroid stimulating hormone receptor antibody (TRAb), thyroglobulin antibody (TGAb), Thyroid peroxidase antibody (TPOAb) is elevated. The pathogenesis of AITD is multifactorial, including genetic susceptibility, pregnancy and various environmental factors (iodine and selenium intake, smoking, acute psychological stress, etc.) and certain drugs (amiodarone, certain immune checkpoints, etc.) Inhibitors, interferons and cytokines) etc. Bacteria and viral infections have long been considered to be the possible culprits of autoimmune diseases. In autoimmune thyroid diseases (AITD), especially in Hashimoto's thyroiditis (HT) and Graves disease (GD), clinical studies related to bacterial and viral infections that may be involved in the pathogenesis and progression of AITD are increasing year by year. However, the risk of autoimmune thyroid disease varies among patients with each specific infection. This meta-analysis estimated the association between various infections and the risk of autoimmune thyroiditis.This meta-analysis estimated the association between Bacterial and viral infections and AITD risk.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 December 2021 and was last updated on 10 December 2021 (registration number INPLASY2021120051).

INTRODUCTION

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METHODS

Search strategy: Literature reporting potential relevance between infection and risk of Autoimmune Thyroid Diseases(AITD) published in PubMed in English from January 1965 to December 2021 was searched. The search strategy was as follows: (Thyroiditis, Autoimmune[MeSH Term]) AND ((((Infection[MeSH Term]) OR Bacteria[MeSH Term]) OR Viruses[MeSH Term]) . EMBASE and Web of Science database was also searched for articles published using similar searching strategy. If any pathogenic microorganism was identified associated with AITD in articles searched using above strategy, a manual search for the related literature between AITD and this pathogenic microorganism species was performed. For example, we identified HP and HCV infection were reported associated with AITD using above terms; then, we searched the databases manually using the following terms: ((Autoimmune Thyroid Diseases) AND Helicobacter pylori), ((Autoimmune Thyroid Diseases) AND Hepatitis C virus). Finally, the reference lists of the included articles were also searched manually to identify additional relevant studies not captured by our database search.

Participant or population: The inclusion and exclusion criteria were as follows: (a) Original studies determining relationship between infection and risk of AITD published in English, including case–control studies, and cohort studies were included for further evaluation, experiment, or studies on animals were excluded; (b) odds radios (ORs; unadjusted), relative risks (RRs), and hazard ratios (HRs) with 95% confidence intervals (CI) should be provided or could be calculated in included studies.

Intervention: Patients with autoimmune thyroiditis infected with various bacteria and viruses.

Comparator: Healthy subjects with matched age, sex, BMI, and dietary habits.

Study designs to be included: Cohort and case–control studies will be included. Healthy subjects with matched age, sex, BMI, and dietary habits.

Eligibility criteria: Patients with autoimmune thyroiditis infected with various bacteria and viruses.

Information sources: Electronic databases：PubMed, EMBASE and Web of Science.

Main outcome(s): The incidence of the above-mentioned autoimmune thyroid disease or the infection rate of various bacteria and viruses.

Quality assessment / Risk of bias analysis: We will use The Newcastle Ottawa Scale (NOS) to evaluate all the included essays, including the trial group selection, comparability, exposure and outcome. The total score ranges from five to nine (with nine is the highest) and a higher score indicating higher quality.

Strategy of data synthesis: A fixed-effect model and a random-effects model will be used to report the results. Statistical heterogeneity will be assessed by the I^2 value, which represents the total variation across different studies. We may choose a random-effects model if the I^2 index>50%, otherwise, a fixed-effects model will be used. Before the data synthesis, we will calculate the ratio of the bacterial percentage of AITD patients and assess the relative abundance value in patients with AITD compared to controls. If possible, we also plan to analyze the influence of bias control and evidence of publication bias by using funnel plots and regression analysis.

Subgroup analysis: None.

Sensitivity analysis: The contribution of publication year, study design,, infected pathogenic microorganisms, methods for detection of infection, and samples used to detect infection to heterogeneity were analyzed by sensitivity analysis. If sensitivity analysis failed to identify the source of heterogeneity, and if there are more than three articles on this pathogenic microorganism, meta-regression was performed to identify the source of heterogeneity.

Country(ies) involved: China.

Keywords: Helicobacter pylori,hepatitis C virus, infection, Malassezia, meta-analysis, Autoimmune Thyroid Diseases.

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