Assessing the Development of Hypothyroidism and Related Disorders Post-H. pylori Infection: A TrinetX Analysis.

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ABSTRACT

Background:
Hypothyroidism is a multifactorial condition with diverse etiologies. Recent studies have proposed a potential association between *Helicobacter pylori* (H. pylori) infection and the development of hypothyroidism or related autoimmune conditions, such as Hashimoto's Thyroiditis (HT). The virulence protein CagA of H. pylori is theorized to play a role in autoimmune disease development. This study aimed to evaluate whether H. pylori infection or its treatment is linked to hypothyroidism or related conditions, such as Hashimotos.

Methods:
A retrospective analysis was conducted using the TrinetX database. Patients were categorized into H. pylori-positive and control groups, with a positive urease breath test confirming H. pylori diagnosis. Additional subgroups divided H. pylori-positive patients into those treated with proton pump inhibitors (PPIs) and those who were not. Propensity matching was used to control for age, sex, and race. Individuals with pre-existing endocrine disorders were excluded. Outcomes assessed included diagnoses of Hashimoto's Thyroiditis or unspecified hypothyroidism, identified via ICD-10 codes.

Results:
The control group showed a significantly higher risk of developing hypothyroidism compared to the H. pylori-positive group (15.4% vs 11.37%, p<0.001). No significant difference was found when comparing risk of developing Hashimotos. Among H. pylori-infected patients, the PPI group (n = 4,267) had a significantly higher risk of developing unspecified hypothyroidism (9.07%) compared to the non-PPI group (7.10%), (p < 0.001).

Conclusions:
This study found a lower risk of developing hypothyroidism in H. pylori-infected individuals compared to controls. This data contrasts previous literature indicating a possible link between the pathogen and development of autoimmune conditions. However, PPI treatment in H. pylori-positive patients was also seen to increase the risk of developing unspecified hypothyroidism. Further studies are needed to clarify the underlying mechanisms and clinical implications of these findings.

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INTRODUCTION

•Hypothyroidism is a multifactorial condition with diverse etiologies, and recent evidence has suggested a possible relationship between **Helicobacter pylori (H. pylori)** infection and thyroid dysfunction[1-2].

•Proposed mechanisms include the virulence protein CagA, which may contribute to autoimmune conditions such as **Hashimoto's thyroiditis (HT)[1]**.

•This study evaluated whether H. pylori infection or its treatment is associated with the development of hypothyroidism or HT.

METHODS AND MATERIALS

•A retrospective cohort analysis was performed using the **TriNetX database**.

•TrinetX is a multicenter database that uses ICD and billing codes to analyze patient data in a confidential manner.

•Patients were divided into H. pylori–positive and control groups, with infection confirmed by urease breath test. Patients in the control group were found through "general visits"

•Subgroup analysis compared H. pylori–positive patients who received **proton pump inhibitor (PPI) therapy** versus those who did not. This was to look for if treatment of H pylori played a role in the development of hypothyroidism.

•Propensity score matching was used to control for **age, sex, and race**, and patients with pre-existing endocrine disorders were excluded.

•Outcomes of interest were diagnoses of **unspecified hypothyroidism** or **Hashimoto's thyroiditis**, identified using ICD-10 codes.

RESULTS

- The **control group showed a significantly higher risk** of developing hypothyroidism compared to the H. pylori-positive group (15.4% vs 11.37%, p<0.001)
- No significant difference was found when comparing risk of developing Hashimoto's
- Among H. pylori-infected patients, the PPI group (n = 4,267) **had a significantly higher risk of developing unspecified hypothyroidism (9.07%) compared to the non-PPI group (7.10%), (p < 0.001)**

FIGURES

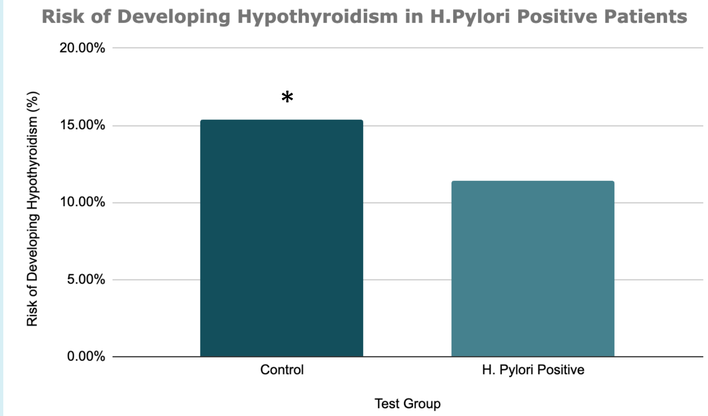

Figure 1: Risk of developing hypothyroidism in H.pylori positive patients.

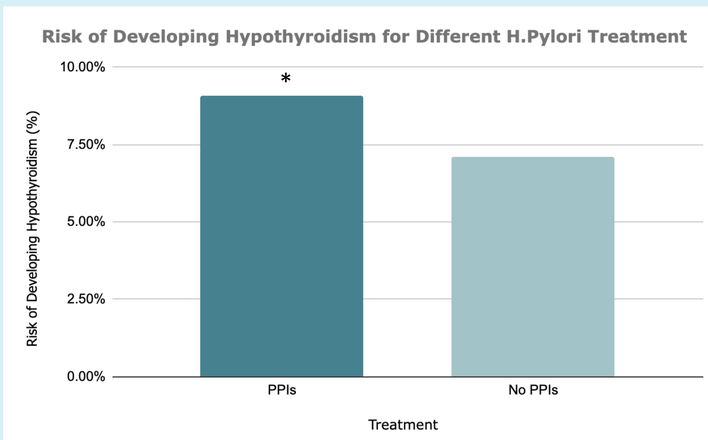

Figure 2: Risk of developing hypothyroidism, Hashimotis type, in patients with and without PPI use.

DISCUSSION

•Contrary to prior hypotheses, H. pylori infection itself was **not associated with an increased risk of hypothyroidism or HT**; in fact, infected individuals showed a lower risk of developing hypothyroidism than controls.

•However, PPI treatment in H. pylori–positive patients was linked to an **elevated risk of hypothyroidism**, raising the possibility that medication effects, rather than infection, may play a role in thyroid dysfunction.

•Potential mechanisms may include altered gastric acidity affecting nutrient absorption (e.g., iodine, selenium) or other indirect effects of long-term PPI use.

•Limitations include retrospective design, reliance on ICD coding, and lack of laboratory confirmation of thyroid disease.

•Future Directions could include further investigating a **possible immunoprotective role** of H.pylori in developing certain autoimmune conditions.

•This study would benefit from applications towards randomized control trials to elucidate if the results are replicable in controlled settings.

CONCLUSIONS

Our findings indicate that there may be a lower risk of developing hypothyroidism in H. pylori-infected individuals compared to controls. While this data contrasts with our hypothesis, in the subtype analysis PPI treatment in H. pylori-positive patients was seen to increase the risk of developing unspecified hypothyroidism. This could indicate that perhaps drug effects may be influencing the relationship between these variables. Still, there remains to be future research into the themes of molecular mimicry, and the potential protective effect of this bacteria on the development of an autoimmune condition like Hashimoto's. Further studies are needed to clarify the underlying mechanisms and clinical implications of these findings.

REFERENCES

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