

The clinical significance of thyroid auto-antibodies in non-thyroidal diseases : What a family medicine physician should know

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Introduction

Epidemiological studies showed that the population has a high immune disease prevalence, and thyroid immune diseases are among the top autoimmune disorders seen in clinical practice. Thyroid autoantibodies are markers for thyroid autoantibodies diseases. They are highly prevalent in these diseases. Investigators noticed an association between Some non-thyroidal conditions with thyroid autoantibodies, and some of the outcomes of these non-thyroidal diseases may be affected by the presence of these thyroid antibodies. Investigators also noticed an association between sociodemographic characteristics such as age, sex, and duration of thyroid or non-thyroidal diseases and thyroid autoantibodies.

Objective

To investigate the association of thyroid autoantibodies with non-thyroidal diseases and their clinical significance, such as the positive or negative impact on the disease outcome.

Methodology

A systematic literature review was done using selection criteria with the help of search questions. Multiple search engines were searched for eligible articles. Articles were filtered based on the inclusion and exclusion criteria. Data were extracted and analysed for clinical or statistical significance between case and control groups in selected studies

Discussion

Thyroid autoantibodies are frequently found in patients with AITDs and subjects without manifest thyroid dysfunction. Thyroid antibodies can be detected in some non-thyroidal illnesses and participate in the pathogenesis of these diseases. These antibodies could be a trigger for inflammatory or allergic reactions. The association of these antibodies with the illness could be a positive or negative correlation. These antibodies could be a prognostic indicator to increase disease-free survival, as in the case of breast carcinoma. Using high-sensitivity tests to detect these antibodies adds a lot to the early detection and improves our clinical management for some diseases, as with the cases of miscarriage. Thyroperoxidase (TPO) and thyroglobulin (Tg) are the primary thyroid antigen that attacks an autoimmune reaction.

Many researchers study the association of these autoantibodies with non-thyroidal diseases such as vit D deficiency, allergic diseases, women's reproductive system diseases, abortion, system lupus erythematosus, and mood disorders. Results from these studies showed a positive association with TPO-Ab, TG-Ab, and these diseases with different degrees. Even some researchers recommend early testing of these autoantibodies in conditions such as cases with female infertility. Age, sex, and geographical distribution were among the risk factors that affected the presence and distribution of these antibodies in participants of these studies.

Results

Eighteen (18) articles fulfilled the inclusion and exclusion criteria; 44.4% were analytical cross-section studies, 5% were prospective studies, 5.5% were meta-analysis studies, 5.5% were case-control studies, and 16.7% were retrospective studies. All studies aimed to find an association between TPO-Ab, TG-Ab, and some non-thyroidal diseases (Vit D deficiency, Allergic diseases, mood disorders, women's reproductive system diseases, abortion, systemic lupus erythematosus, rheumatoid disease, Celiac disease, Type 1 diabetes, and breast cancer. The ORs in the included studies were > 1, and the confidence intervals did not cross 1, which means both clinical (favor positivity in case groups) and statistical (existing of difference between case and control groups) significance. All "r" results in included studies $r > 0$ but $< +1$ which indicate a positive correlation. In the included meta-analysis study, the Foster Plot graphs showed that the included studies showed a favourable positive effect on the positivity of thyroid autoantibodies. The I^2 "value, which is an indicator for heterogeneity of the studies included in the meta-analysis, was high in the included research (>50%), which indicates heterogeneity of the included study. TPO-Ab was a favourable prognostic indicator in cases of breast cancer. Relative risk (RR) was used to assess the disease-free survival rate in subjects with breast carcinoma. The survival rate between patients with TPO-Ab > 0.3u/ml and <0.3u/ml was statistically significant (P value 0.016), and relative risk = 3.46. Relative risk > 1 means the specific factor (presence of high TPO-Ab > 0.3u/ml increases the disease-free survival).

Conclusions

Thyroid autoantibodies are not exclusively markers of thyroid autoimmune diseases but can also be markers and indicators of non-thyroidal illnesses. Their presence could be either a favourable prognostic indicator, as with breast carcinoma cases or unfavourable prognostic, as with abortion.

Summary of data extraction

Author	type	Date of publication	Population	Disease investigated	Statistical tools
Carta et al	Analytic Cross-sectional study	2004	222 adults	Mood disorders	Prevalence, OR, CI 95%, P value, MVLR
Snijders et al	Analytic Cross-sectional study	2020	1021 case group, 373 control group, adult	Bipolar disorders	OR, P value
Shin et al	Retrospective study	2014	304 psricipants. adults	Vit D deficiency	P value, correlation (r)
Darban et al	Analytic cross section study	2022	35 case group, 35 control group. adults	Vit D deficiency	OR, CI 95%, P value
Zhang et al	Analytic cross sectional study	2022	217 case group, 217 control group. adults	Allergic diseases	P value, CI 95%
Ismail et al	Case control study	2020	25 case group, 25 control group. Children	Bronchial asthma	P value, correlation (r).
Levy et al	Cohort prospective study	2003	187 . children	Chronic urticaria	Incidence rate
Zhang et al	Analytic cross sectional study	2022	1100 case group, 1100 control group	Chronic spontaneous urticaria	OR, P value, correlation (r)
Singh et al	Cohort retrospective study	1995	487 participants. Adult women	Reproductive failure	P value
Janssen et al	Cohort prospective study	2004	175 case group, 168 control group.	Polycystic ovary	Incidence rate, P value
Wang et al	Cohort retrospective study	2018	121 case group, 408 control group, Adult women	Female infertility	Incidence rate, P value
Stagnaro et al	Cohort Retrospective study	1990	552 adult women	Miscarige in at risk pregnancy	Prevalnce, P value
Pan et al	Meta-analysis	2015	1076 case group, 1661 control group	Systemic Lupus Erythematous (SLE)	OR, P value, CI 95%
Sieiro et al	Cohort Prospective study	2004	587 participants	Abortion	P value, CI 95%, incidence. P value, RR
Smyth et al	Analytic cross sectional study	1998	478 case group, 222 control group	Breast cancer	P value, r, 95% CI
Sharifi, Ghasemi and Mousavinasab, 2008	Analytic cross sectional study	2008	91 case, 163 controls	Type 1 diabetes	P value, r, 95% CI
Kalyoncu and Urganç, 2015	Cohort prospective study	2015	67 case . children	Celiac disease	P value
Roldan et al, 2012	Analytical cross sectional study	2012	800 case. Adult	Rheumatoid disease	OR, P value, 95% CI

OR=Odds ratio, CI 95%= Confidence Interval 95%, P value, MVLR = Multivariate Logistic Regression, RR=Relative Risk r=correlation coefficient

Limitations

Exclusion of articles not written in English, is one of the limitations may introduce some bias into this research. Omit articles not written in English or have English translation may led to omission of relevant data.

Exclusion of non open articles, articles without free full texts, gray zone articles may affect the selection of articles.

Key message for family medicine physicians

✓ In inclusion, thyroid autoantibodies were not an exclusive indicator for thyroid diseases. However, they became clinical indicators of other non-thyroidal diseases, and their clinical significance must be assessed and followed.

References

- Fröhlich, E. and Wahl, R., 2017. Thyroid autoimmunity: role of anti-thyroid antibodies in thyroid and extra-thyroidal diseases. *Frontiers in immunology*, 8, p.521.
- Atkinson, L.Z. and Cipriani, A., 2018. How to carry out a literature search for a systematic review: a practical guide. *BJPsych Advances*, 24(2), pp.74-82.
- Sinclair, D., 2006. Clinical and laboratory aspects of thyroid autoantibodies. *Annals of clinical biochemistry*, 43(3), pp.173-183..