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Association between Anti-Thyroid Peroxidase Antibody and Asthma in Women

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ABSTRACT

About 8% of the general population suffers from autoimmune diseases, from which 78% are women. One of the most important causes of thyroid diseases is autoimmunity in origin, and it seems that people with thyroid diseases present more signs of asthma. This study was therefore designed to investigate the frequency of autoimmune thyroid diseases in women suffering from bronchial asthma.

In a cross-sectional study, 100 women with asthma and 100 women as control group were tested for thyroid function and anti-thyroid peroxidase antibody (anti-TPO Ab) measurements. The asthmatic patients were selected based on having chronic cough, dyspnea, wheezing and clinical examination of the chest. The diagnosis was confirmed by pulmonary function tests. Blood tests were done by electrochemiluminescence immunoassay method.

No hyperthyroid patient was found in either group. Serum TSH and Total T4 levels were not statistically different between the two groups, but serum anti-TPO Ab levels in women with asthma (74±13.6 IU/ml) was significantly higher than control group (45.24±10.56 IU/ml). After adjusting the effect of age and BMI, the relationship between asthma and anti-TPO Ab (>50 IU/ml) was statistically significant (OR=3.3, P<0.01).

Positive anti-TPO Ab in asthmatic patients may show presence of a hidden autoimmune thyroiditis in these patients. We suggested checking asthmatic patients for thyroid diseases.

Keywords: Anti-thyroid peroxidase antibody; Asthma; Thyroid function test; Women

INTRODUCTION

Asthma is a syndrome of bronchial obstruction due to sub acute inflammation in which airways are highly responsive to a vast range of stimulators, causing reduction of air flow, dyspnea, wheezing, and coughing.[1] In the U.S., about 20 million people suffer from asthma, which need 12.7 million visits yearly. It is estimated that these patients bear about $16 million in 2001 and caused 14.7 million days absence from school.[2] About 8% of the populations suffer from autoimmune diseases, 78% of whom are females. This sex difference in frequency of autoimmune diseases is

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shown in Sjogren's syndrome, systemic lupus erythematosus, scleroderma and autoimmune thyroid disease in which the rate is higher in females than in males.[3] Thyroxin (T4) and triidothyronin (T3) hormones from thyroid glands have vital effects on cell growth, differentiation and development, and also regulate body metabolic and thermogenic homeostasis[4]. Thyroid dysfunction causes extensive metabolic and enzymatic changes in cell level and causes deviation from normal body activities.[5] It has been shown that with the increase of cell adenosine triphosphate (ATP) production cycle activity in hyperthyroidism, the asthma signs in patients increases and the treatment of hyperthyroidism in these patients reduces severity of their asthma.[6,7] The pathogenic mechanism for relationship between thyroid dysfunction and severity of asthma signs is not clearly understood. It is hypothesized that thyroid hormones change the prostaglandin, leukoterian, and catecholamine levels in tissue and circulation; intracellular cyclic adenosine monophosphate (cAMP) level and affect bronchial muscle contractile properties.[8] As asthmatic patients are more reactive to exogenous antigens, it is probable for them to be hyper-reactive to endogenous antigens as well.[9] Some studies have shown that hypothyroidism ameliorates and hyperthyroidism exacerbates bronchial asthma.[10,11] The study of Toru Hikta and colleagues on 13 asthmatics showed that aminophyline injection caused catecholamine release, B2 adrenergic receptor stimulation, thyroid releasing hormone (TRH) release from hypothalamus and resultant increase in thyroid stimulating hormone (TSH) and T4. They recommended hypophysis-thyroid axis assessment in asthmatic patients.[12]

Behera et al. found more therapeutic response to bronchodilator fenotrol after treatment of hyperthyroidism in 15 patients.[13] Hault et al. showed that in asthmatic hyperthyroid patients, the prostaglandin metabolism is lower. Therefore, increase in prostaglandin (PG) E2 and PGF2α levels which are synthesized in lungs caused increase in asthma signs in these patients.[6]

It is also shown that in 15 asthmatic children, theophylin caused a temporary increase in T4 and due to transformation of T4 to T3, there was an increase in side effects of theophyline.[14]In this study, we investigated the prevalence of hypo- and hyper-thyroidism and blood levels of anti-thyroid peroxidase antibody (anti-TPO Ab) in 100 women suffering from bronchial asthma compared to 100 non asthmatic women.

MATERIALS AND METHODS

The study was approved by ethics committee of Kerman University of Medical Sciences (KUMS) with permission number of KA/89/24. In this descriptive cross-sectional study, 100 women over 18 years of age with asthma disease who attended a specialty clinic, were selected. Exclusion criteria were having a diagnosis of chronic obstructive pulmonary disease (COPD), connective tissue diseases, congestive heart failure, chronic renal failure or positive history of definite thyroid diseases or being under treatment. Pregnant and smoking women were also excluded. Control group consisted of 100 women selected from people participated in a field trial study with a large sample size in the city about prevalence of coronary artery disease risk factors. This group had no signs of asthma disease in addition to all the above exclusion criteria. According a check-list, some basic/demographic information such as age, height (m), weight (kg), body mass index (BMI) were gathered.

The asthmatic patients were selected based on having chronic coughing, dyspnea, wheezing and clinical examination of the chest. The diagnosis was confirmed by pulmonary function tests with spirometer (spirolab 3, MIR Co, Italy).

If the forced expiratory volume in one second (FEV1) after 15 minutes of bronchodilator administration (two puffs of salbutamol inhaler) was increased by 12% or 200 ml, the patient was considered as asthmatic.[1] Asthma severity was graded based on guidelines for diagnosis and treatment of asthma.[15] Four groups consisting of: 1) mild intermittent, 2) mild persistent 3) moderate persistent and 4) severe persistent were considered. Blood was collected for TSH, Total T4 and anti-TPO Ab measurements after taking informed constant from the participants. Blood samples were centrifuged after 20 min of collection and the sera were freezed at -20°c until the end of sample collection (max 3 months). Blood tests were done by electrochemi luminescence immunoassay method (ELYCSE 2010, Roche Company, Germany country). Hyperthyroidism was based on TSH<0.01 IU/ml (normal range 0.5-5 IU/ml) and Total T4>12 µg/dl (normal range 4.5-12 µg/dl). Hypothyroidism was based on TSH>10 IU/ml and Total T4<4.5 µg/dl.[4] Anti-TPO Ab>50 IU/ml was considered as positive.

Table 1. Demographic characteristics and thyroid function test results of the study groups

Variable	Group with asthma (n = 100)	Control group (n = 100)	*P value*
Age	44.82±9.8*	33.06±8.5	<0.001
Height	155.38±11.9	161.11±6.7	<0.001
Weight	72.40±10.7	66.67±13.4	<0.001
BMI	33.36±26.8	25.68±4.9	<0.001
TSH	5.36±14.5	2.90±2.1	0.11
Total T4	8.23±1.6	7.97±1.8	0.45
Anti-Tpo Ab (IU/ml)	74±13.6	45.24±10.56	<0.01
Anti-Tpo Ab categories			
<50	72**	90	
51-200	18	3	
201-500	6	6	<0.01
>500	4	1	

* data are presented as Mean±standard deviations ** data are in both N and %

Statistical analysis: The sample size was calculated by comparison of two proportions with α=0.05, β=20% (power of 80%) that it was obtained equal to 100 sample for each group. Data are presented as Mean ± standard deviations (S.D.) for continuous variables and absolute and relative frequencies for categorical variables. To compare continuous variables between two groups, unpaired t test (for variables with normal distributions) and Mann-Whitney test (for variables with non-normal distributions) were used. Pearson chi-square test and Fisher Exact test (if necessary) were used to compare categorical variables and also to determine the association between severity of asthma and anti-TPO Ab levels. Anti-TPO Ab was considered as both continuous and categorical variables and statistical analyses were performed for them. Anti-TPO Ab was categorized in four categories of <50, 50-200, 200-500 and >500 IU/ml.[16, 17] In another case, anti-TPO Ab was categorized in two groups of negetive (≤50 IU/ml) and positive (>50 IU/ml). Based on this stratification, to adjust confounder variables (such as age and BMI) and to determine the strength of the associations, multivariate logistic regression (to calculate the odds ratio (OR)) was used. Statistical analysis was performed by SPSS version 15. *P* values <0.05 were considered significant.

RESULTS

No hyperthyroid person was found in either group of with asthma or without (control) asthma. There were six hypothyroid persons, five of whom (5%) were in group with asthma and one (1%) in control group, but this difference was not statistically significant (p>0.05). Among these five patients, three women were in moderate and severe persistent asthma sub-groups. The basal demographic characteristics of two groups along with the results of thyroid function tests (TSH and Total T4) are presented in Table 1. Women in group with asthma had a higher age and BMI in comparison with control group (p<0.05). The thyroid function tests were not statistically different between the two groups (p<0.05).

However, the anti-TPO Ab levels was significantly higher in group with asthma in comparison with control group (74±13.6 and 45.24±10.56 IU/ml, respectively and P<0.01). Out of 100 women with asthma, 72% had anti-TPO Ab≤50 IU/ml and this value for control group was 90%. About 18% of women in asthma group and 3% of women in control group were in category of 51-200 and this difference was statistically significant (p<0.01), (Table 1).

Table 2. Comparison of frequency of anti-TPO Ab abnormality and hypothrodism in study groups

Variable	Control group	Group with asthma	*P* value
Anti-Tpo Ab>50 IU/ml	10	27	0.002
Hypothyroids	1	5	0.09

Table 3. Relationship between severity of asthma and anti-TPO Ab serum levels

Asthma	Total	Mild intermittent	Mild persistent	Moderate persistent	Severe persistent	*P value*
Anti-Tpo Ab≤50 IU/ml (negative)	72 (72.7%)	7 (63.6%)	8 (61.5%)	29 (80.6%)	28 (70%)	0.54
Anti-Tpo Ab>50 IU/ml (positive)	37 (27.3%)	4 (36.4%)	5 (38.5%)	7 (19.4%)	12 (30%)	

A positive anti-TPO Ab serum level (>50 IU/ml) was found in 27% of women with asthma and 10% of control groups (Table 2) and this difference was statistically significant (p<0.002). After adjusting the effect of age and BMI, the result of multivariate logistic regression showed that the odds of having positive anti-TPO Ab (>50IU/ml) in women with asthma was 3.3 times more than control group (OR=3.3, 95%CI=1.47-7.2, p=0.02).

There was no association between severity of bronchial asthma and anti-TPO Ab level (p= 0.54, Table 3). Among women with asthma, 27% had allergic rhinitis and 16% urticaria.

DISCUSSION

In the present study no significant association was found between thyroid function disorders and bronchial asthma, as no hyperthyroid was found among 100 asthmatic patients. There was not found a significant difference in the term of prevalence of hypothyroidism between test group (5%) and control group (1%).The results were in agreement with findings of Abd EL Aziz et al. on 40 patients (including 20 bronchial asthma and 20 allergic rhinitis patients) in whom thyroid function tests (TSH, T4, T3) were not found to be statistically different between test and control groups.[18] In contrast, in the study of Jerez et al[19] on 49 asthmatics that were not responsive to anti-asthmatic treatments, the prevalence of hypothyroidism was higher in the test group. This difference in results may be due to higher sample size in the present study.

In the study of Rebecca on 90 asthmatic patients with major depression no correlation was found between TSH levels and depression but significant relationship was found between TSH and asthma control questionnaire (ACQ) results.[20] In the present study, no significant association between TSH level and asthma was found.

In the study of Landyshev et al on 16 patients with severe bronchial asthma, in which TSH, T4 and T3 were measured every 6 hours for 48 hours, T3 was found to be higher than normal, while T4 dropped during night period.[21] This finding is not consistent with our results in this study, in which no association was found between thyroid function disorders and asthma. Unfortunately we did not measure the level of T3 in this study. Our results are consistent with the study of Lindberg et al in which no association was found between TSH, T3 and T4 and bronchial asthma.[9] Regarding the association between thyroid autoantibody level and asthma in few studies, results similar to the results of this study have been reported.[9,18] In the study of Quintero et al on 24 patients with chronic asthma, the level of anti globulin was found to be 10 times more compared to patients with non pulmonary chronic diseases.[22] The higher BMI found in asthmatic patients of present study is also reported by Hancox[23] and Nystad.[24]

The association between anti-TPO Ab and bronchial asthma found in the present study may show abnormal immunologic reasons and presence of hidden autoimmune thyroiditis in these patients, but this autoimmunity had no effect on serum level of thyroid hormones. Although thyroid autoimmune diseases are common, positive thyroid peroxidase antibody is not necessarily a sign of disease. This antibody is found in all patients with thyroid Hashimoto and 70% of patients with Graves disease and the presence of this antibody may show thyroid inflammation and increased risk of autoimmune thyroid diseases in these persons. Now it is accepted that there is relationship between bronchial asthma and autoantibody against thyroid, however there is a question that is this relationship pathologic or it is an association with autoimmune reaction?

Limitations of the study include performing the study on females, small sample size and some confounder factors such as known and unknown antigens which could affect the anti-TPO Ab.

CONCLUSION

Based on the findings of the present study we propose patients with asthma to be checked in their treatment period for their thyroid function tests.

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REFERENCES

1. Barnes JP. Asthma In: Harrison's Internal Medicine. 17th ed, McGraw Hill, New York, NY, 2008:1596-607.
2. Apter AJ, Weiss ST. Asthma: Epidemiology In: Fishman AP: Fishman's Pulmonary Disease and Disorder's. 4th ed. McGraw Hill, New York, NY, 2008:787-98.
3. Whitacre CC. Sex differences in autoimmune disease. Nature Immunology 2001; 2 (9):777-8.
4. Jameson LJ, Weetman AP. Disorders of the thyroid gland. In: Harrison's Internal Medicine. 17th ed, McGraw Hill, New York, NY, 2008:2224-47.
5. Saarinen S, Olerup O, Broome U. Increase in frequency of autoimmune disease in patients with primary sclerosing cholangitis. Am J Gastroentral 2000; 95(11) 3195-9.
6. Hoult JR, Moor P. Thyroid disease, asthma and prostaglandins. BMJ 1978; 1(6109):366.
7. Settipane GA, Schoenfeld E, Hamolsky MW. Asthma and hyperthyroidism. J Allergy Clin Immunol 1972; 49(6):348-55.
8. DiNicola AF. Might hyperthyroxinemic states exacerbate bronchial asthma by stimulating the production of leukotrienes C4, D4 or E4? Med Hypotheses 1983; 10(2):199-206.
9. Lindberg B, Ericsson UB, Fredriksson B, Nilsson P, Olsson CM, Svenonius E, et al. The coexistence of thyroid autoimmunity in children and adolescents with various allergic diseases. Acta Pediatr 1998; 87(4):371-4.
10. Rowe MS. Thyroid hormones and asthma. Ann Intern Med 1991; 114(1):97.
11. Ayers J, Clark TJH. Asthma and Thyroid. Lancet 1981; 2(8255):1110-1.
12. Hikta T, Fukutani K, Yamamoto Y, Yoshimizu N, Sasaki T. Effect of aminophylline injection on the pituitary – thyroid axis in asthmatics. Jpn J Med 1989; 28(3):303-8.
13. Behera D, Roy R, Dash RJ, Jindal SK. Airway Response to inhaled fenoterol in hyperthyroid patients before and after treatment. J Asthma 1992; 29(6):369-74.
14. Hiratani M, Muto K, Oshida Y, Ito S, Kasei M, Ueda S, et al. Effect of sustained-release theophylline administration on pituitary -thyroid axis. J Allergy Clin Immunol 1982; 70(6):481-5.
15. National Asthma Education and Prevention Program (NAEPP). Expert panel report 3: guidelines for the diagnosis and management of asthma. Bethesda (MD): National Heart, Lung, and Blood Institute; 2007 Aug. p. 213-76.
16. Moayeri H, Rabbani A. Prevalence of autoantibodies to thyroid peroxidase and autoimmune thyroid disease in type 1 diabetes mellitus. Acta Medica Iranica 2004; 42(4):267-71.
17. Sharifi K, Ghasemi L, Mousavinasab N. Thyroid function and anti-thyroid antibodies in Iranian patients with type 1 diabetes mellitus: influences of age and sex. Iran J Allergy Asthma Immunol 2008; 7(1):31-6.
18. Abd EL-Aziz MF, Rafaat MM, Sabry IM, Yousef M, Mandour A. Study of thyroid auto-antibodies in patients with bronchial asthma and allergic rhinitis. Thyroid Science 2010; 5(2):CLS1-5.
19. Jerez FR, Plaza V, Tárrega J, Casan P, Rodríguez J. Thyroid function and difficult to manage asthma. Arch Brounconeumol 1998; 34(9):429-32.[Abstract]
20. Rebecca J. Oppedal, David A. Khan, E Sherwood Brown. Hypothyroidism in patients with asthma and major depressive disorder. Prim Care companion J Clin Psychiatry 2007; 9(6):467-8.
21. Landyshev IS, Mishchuk VP, Lysenko VA, Petrov AV. Circadian rythms of hypophysis-thyroid hormones secretion in patients with bronchial asthma. Terapevticheskii Arkhiv 2006; 72(3):13-5.
22. Quintero JM, Burrell RG, Cather CH, Wymer B, Baise R. Detection of antibodies to sinus tissue in chronic bronchial Asthma. J Allergy 1966; 37(2):84-9.
23. Hancox RJ, Milne BJ, Poulton R, Taylor DR, Greene JM, McLachlan CR, et al. Sex difference in the relation between body mass index and asthma and atopy in a birth cohort. Am J Resp Critical Care Med 2005; 171(5):440-5.
24. Nystad W, Meyer HE, Nafstad P, Tverdal A, Engeland A. Body mass index in relation to adult asthma among 135000 Norwegian men and women. Am J Epidemiol 2004; 160(10):969-76.