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Iron deficiency in women with thyroid-specific autoantibodies: A case control study

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Abstract

Autoimmune thyroid diseases are multifaceted conditions in which the thyroid gland is infiltrated by lymphocytes, resulting in the production of thyroid-specific auto-antibodies against thyroid peroxidase (TPOAb) and thyroglobulin (TGAb). Iron deficiency is a common nutritional deficiency and has multiple adverse effects on thyroid metabolism. The association between iron status and thyroid autoimmunity has not been well-evaluated. This retrospective study aimed to determine whether the frequency of iron deficiency was higher in patients with thyroid autoimmunity than in healthy individuals with negative thyroid autoantibodies. One-hundred-and-eighty female patients with positive thyroid auto-antibodies and 81 healthy controls were involved in the study. Hemoglobin, hematocrit, mean corpuscular volume (MCV), iron, thyrotropin (TSH), TPOAb, TGAb, free-T4, vitamin B12, ferritin and transferrin saturation (TS) were recorded. TSH, TPOAb and TGAb levels were significantly higher, while hemoglobin, hematocrit, MCV, ferritin, iron and TS were significantly lower in the patient group (all, $p<0.05$). Patients with thyroid autoimmunity had significantly higher frequency of lower levels of hemoglobin, iron, ferritin, MCV and TS than healthy controls (all, $p<0.005$). Correlations were found inversely between TPOAb and serum ferritin, iron, and TS levels, and also positively between TGAb and creatinine levels in the patient group. In conclusion, we found increased prevalence of iron deficiency in female patients with thyroid autoimmunity. Patients with autoimmune thyroid diseases were found to be at higher risk of iron deficiency development.

Keywords: anti-thyroglobulin antibody, anti-thyroid peroxidase antibody, ferritin, hemoglobin, iron

1. Introduction

The thyroid gland plays an important role in the regulation of multiple functions, such as metabolic rate, energy expenditure, general homeostasis and the use of other hormones and vitamins in the body. It is also the organ most affected by autoimmune conditions (1). In autoimmune thyroid diseases, the thyroid gland is infiltrated by auto-reactive lymphocytes which cause the production of circulating thyroid-specific autoantibodies. Hashimoto thyroiditis is the most common form of autoimmune disease worldwide and is the most common cause of primary hypothyroidism in iodine-sufficient regions (2). It is more prevalent among women and the 40-60 years age group. The etiopathogenesis of Hashimoto's disease remains uncertain, but it is suggested to be caused by various complex interactions between genetic susceptibility, environmental and nutritional factors, and immune disorders (3). It is frequently accompanied by other autoimmune disorders, such as Celiac disease, chronic autoimmune gastritis, and type I diabetes mellitus (4). Hashimoto thyroiditis is characterized by clinical hypothyroidism and the presence of auto-antibodies against thyroid peroxidase (TPOAb) and thyroglobulin (TGAb) (2). TPO is the key enzyme that oxidizes iodide to iodine that will be incorporated into thyroglobulin for the synthesis of thyroxine (T4) or triiodothyronine (T3) (5). TPOAb, the predominant antibody in autoimmune hypothyroidism, has been reported to be present in over 90% of patients and serves as a useful biomarker to identify disease without a need for thyroid biopsy or surgery (1).

Nutritional factors, including iodine, selenium, zinc, vitamin B12, vitamin D and iron may be associated with thyroid dysfunction (6). Iron deficiency is the most common nutritional disorder. In addition to being a very common cause of anemia, iron deficiency results in multiple adverse effects on thyroid metabolism by reducing activity of heme dependent TPO and interfering with the synthesis of thyroid hormones (7). However, the association between iron status and thyroid autoimmunity has not been well assessed. The present study aimed to evaluate whether the frequency of iron deficiency anemia was more common in patients with thyroid autoimmunity than in the individuals without thyroid disease.

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2. Materials and Methods

This was a retrospective single center study that was carried out from January 2013 to May 2015 in the Endocrinology and Metabolic diseases Departments of Göztepe Training and Research Hospital, Medeniyet University, Istanbul, Turkey. A total of 554 patients with positive TPOAb and/or TGAb who were admitted to outpatient clinics were selected to be included in the study. The study group consisted of euthyroid or subclinical hypothyroid Hashimoto patients irrespective of their treatment status with levothyroxine. Patients younger than 18 and those older than 70 years old, patients with infections, chronic diseases (including diabetes mellitus and hypertension), malignancy, liver, kidney or cerebrovascular diseases, gastrointestinal disorders (including oesophagitis, erosive gastritis, peptic ulcer disease, inflammatory bowel disease and hemorrhoids), endocrine disorders (Cushing syndrome, acromegaly, adrenal insufficiency), autoimmune diseases (systemic lupus erythematosus, rheumatoid arthritis) were excluded from the study. In addition, pregnant women, patients with alcohol or substance abuse, those receiving medications other than levothyroxine, patients diagnosed with hypochromic microcytic anemia (other than iron deficiency: thalassemia, sideroblastic anemia) were excluded from the study. A total of 63 patients were excluded from the study with regard to exclusion criteria. Twenty-four patients were not involved to the study, due to taking iron supplementation at screening. Thirteen patients were excluded from study because they had autoimmune diseases including celiac disease and autoimmune chronic gastritis, which are co-morbidities with Hashimoto's disease and could affect the iron status (4). Twenty-six patients were excluded from the study in terms of menstrual disorders. Previous studies have shown that gender differences could affect iron status, so we included only female patients to attain a homogenous patient cohort (8). A final group of 180 female patients with positive thyroid auto-antibodies were included in the study. The control group consisted of 81 healthy women admitted to the hospital for routine examination who were euthyroid or had subclinical hypothyroidism but had no thyroid auto-antibodies. The study protocol was approved by the Research Ethics Committee of Göztepe Training and Research Hospital, Medeniyet University (2015/0023).

According to the World Health Organization criteria, anemia is defined as a hemoglobin value of <12 g/dL in non-pregnant women (9). Patients with serum ferritin level <12 ng/mL, serum iron level <50 µg/dL, MCV <80 fL and transferrin saturation <16% were considered as having abnormal results (10).

Demographic characteristics, co-morbidities and laboratory findings were retrospectively retrieved from patient charts. Hemogram parameters, including hemoglobin (Hb), hematocrit (Hct) and mean corpuscular volume (MCV) were measured with CELL-DYN 3700 System (Abbott Laboratories, IL, USA). Blood biochemistry parameters, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine, blood urea nitrogen (BUN), iron, and unsaturated iron binding capacity (UIBC) were determined with spectrophotometric methods using Abbott Architect c8000 autoanalyzer (Abbott Laboratories, IL, USA). Serum thyrotropin (TSH), TPOAb, TGAb, free T4, vitamin B12 and ferritin levels were measured with the chemiluminescent microparticle immunoassay method by Abbott i2000 immunochemistry analyzer (Abbott Laboratories, IL, USA). Results above the manufacturer's reference limit for TPO-Ab and Tg-Ab were considered positive (TPOAb 5.61 IU / ml; TGAb 4.11 IU / ml). All blood samples were obtained from each patient in the morning and examined within less than one hour after the sampling. Each of the biochemical analyses were performed with the same analyzers and the same test kits in the central laboratory of our hospital.

2.1. Statistical Analysis

Data were presented as mean ± standard deviation or median (minimum-maximum) for continuous variables according to normality of distribution for quantitative variables, and frequency (percentage) for categorical variables. In comparison of quantitative data, Student's t-test was used for comparing two groups of normally distributed variables, and Mann-Whitney U test was used for comparing non-normally distributed variables. The Pearson chi-squared test, Fisher's exact test and Yates' continuity correction (Yates corrected Chi-square) were used to compare categorical variables. The Pearson correlation analysis was performed to evaluate the relationship between the variables. All analyses were performed using NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA). A p value <0.05 was accepted as statistically significant.

3. Results

One-hundred-and-eighty female patients with positive TPOAb and TGAb and 81 healthy women were included in the study. The median age was 43.2±13.1 years in the study group and 46.1±15.3 years in the control group (p=0.143). TSH levels were significantly higher in the patient group (p=0.001). Hemoglobin, hematocrit, MCV, ferritin, iron and transferrin saturation values were significantly lower in patients with positive TPOAb and TGAb (p<0.05 for all). No differences were found between the two groups regarding AST, ALT, vitamin B12, and creatinine levels (p<0.05 for all). Demographic characteristics and laboratory values of the patient and control groups are shown in Table 1.

Table 1. Mean age and laboratory values of the patient and the control groups

	Patients (*n*=180)	Controls (*n*=81)	*p*-value
Age (years)	43.2±13.1	46.1±15.3	0.143
TSH (µIU/mL)	2.7±3.0	1.8±1.1	**0.001**
Free T4 (ng/dL)	1.07±0.30	1.04±0.23	0.267
TPOAb (IU/mL)	107 (0.5-1095)	0.5 (0.5-3.2)	**0.001**
TGAb (IU/mL)	26.58 (0.79-1000)	1.1(0.27-4)	**0.001**
Hemoglobin (g/dL)	12.2±1.3	12.7±1.2	**0.003**
Hematocrit (%)	36.4±3.4	37.7±3.3	**0.004**
MCV (fL)	83.2±7.0	84.8±5.3	**0.037**
Iron (µg/dL)	59.5±33.4	71..6±32.7	**0.007**
UIBC (µg/dL)	285.9±70.6	269.7±71.6	0.092
Ferritin (ng/mL)	24.9±30.9	37.8±33.1	**0.004**
Vitamin B12 (pg/mL)	351±188	377±287	0.457
AST (U/L)	17.8±8.2	18.8±10.4	0.433
ALT (U/L)	17.9±11.0	20.6±13.8	0.126
Creatinine (mg/dL)	0.8±0.5	0.7±0.1	0.059
BUN (mg/dL)	22.5±7.7	26.1±10.0	**0.005**
Transferrin saturation (%)	23.2±16.8	29.3±16.9	**0.008**

TSH: Thyrotropin, T4: Thyroxine, TPOAb: Thyroid peroxidase antibodies, TGAb: Thyroglobulin antibodies, MCV: Mean corpuscular volume, UIBC: Unsaturated iron binding capacity, AST: Aspartate amino-transferase, ALT: Alanine amino-transferase, BUN: Blood urea-nitrogen.

According to the World Health Organization criterias, 83 (46%), 78 (43%), and 79 (44%) TPOAb and TGAb positive patients were found to have abnormal levels of iron, hemoglobin, and ferritin, respectively. TPOAb- and TGAb-positive patients had a significantly higher frequency of having abnormal values in hemoglobin, iron, ferritin, MCV and transferrin saturation compared with the control subjects ($p<0.005$ for all) There is also a significant relationship between TPOAb level and serum iron, ferritin, and transferrin saturation values. (Table-2). When we divided the study group according to serum ferritin levels (for determination of iron deficiency; serum ferritin levels <12 ng/mL), we did not observe any differences between the groups ($p=0.120$ and $p=178$, respectively) (Table 3).

Table 2. Number and percentage of individuals with abnormal levels of MCV, ferritin, transferrrin saturation in patient and control group

	Patients (*n*=180)	Controls (*n*=81)	*p*-value
Low MCV (<80 fL)	53 (29%)	14 (%17)	**0.001**
Low Ferritin (<12 ng/mL)	79 (44%)	19 (%23)	**0.001**
Low Transferrin saturation (<16%)	80 (44%)	19 (%23)	**0.001**
Low Serum Iron (<50 µg/dL)	83 (46%)	22 (%27)	**0.001**
Decreased Hemoglobin (<12 g/dL)	78 (43%)	21 (%26)	**0.001**

In correlation analyses, we found negative correlations between TPOAb and serum ferritin, iron, and transferrin saturation levels in the patient group (Table-4). Also, there was a positive correlation between TGAb and serum creatinine level in patients.

4. Discussion

This study aimed to determine the frequency of iron deficiency anemia in patients with positive thyroid-specific antibodies and to compare results with healthy individuals. We found decreased levels of hemoglobin, hematocrit, MCV, iron, ferritin, and transferrin saturation in TPOAb and TGAb positive patients compared to control subjects. Our results demonstrated higher frequencies of abnormal levels of hemoglobin, iron, and ferritin in patients with thyroid auto-antibodies than the control subjects. We also observed a significant correlation between TPOAb level and serum iron, ferritin, and transferrin saturation values.

Iron is an essential micronutrient and is contained in hemoglobin, myoglobin, and numerous iron-containing enzymes; therefore, it is involved in various metabolic processes including oxygen transport and storage, oxidation-reduction reactions, electron transfer, ATP production, DNA synthesis (11). Iron deficiency is a highly prevalent nutritional deficiency worldwide, with the most common results being anemia, decreased oxygen transport and impaired activity of iron-containing enzymes. Iron metabolism is related with the synthesis and metabolism of thyroid hormone. Several animal and human studies have demonstrated that iron deficiency may lower circulating levels of T3 and T4 and may also decrease peripheral conversion of T4 to T3 (12). TPO is the unique heme-dependent enzyme required for thyroid hormone synthesis through iodide oxidation into iodine and incorporation of iodine to the tyrosyl residue of thyroglobulin for formation of mono-iodotyrosine and di-iodotyrosine (13). TPO becomes active at the apical surfaces of thyrocytes only after binding a prosthetic heme group (14). Iron deficiency may decrease TPO activity, causing lower T4 production –and higher serum

TSH levels due to negative feedback. Iron deficiency triggers ineffective erythropoiesis and reduced oxygen transport to different tissues, which may lead to hypoxia and impaired enzymatic activity in a variety of enzymes, including the enzymes contributing to thyroid metabolism (15). Iron deficiency can also increase in-vitro hepatic reverse triiodothyronine deiodination, suggesting that thyroid hormones tend to be metabolized in inactivating pathways under iron-deficient conditions (16). Therefore, iron sufficiency is important for thyroid hormone synthesis.

Table 3. Comparison of thyroid functions in study and control groups with different ferritin levels

	Patients with iron deficiency* in study group (n=79)	Patients with iron deficiency in control (n=19)	*p* value	Patients with non-iron deficiency in study group (n=102)	Patients with non-iron deficiency in control group (n=62)	*p* value	*p* value**
TSH	2.87±3.03	1.73±1.12	**0.010**	2.56±3.00	1.72±1.11	**0.012**	0.449
T4	1.05±0.25	1.03±0.10	0.507	1.09±0.33	1.04±0.26	0.248	0.306
TPOAb	297.54±337.79	0.55±0.12	**0.001**	222.75±292.97	0.69±0.62	**0.001**	0.120
TGAb	125.18±234.87	1.53±1.09	**0.001**	82.19±177.76	1.45±0.94	**0.001**	0.178

TSH: Thyrophin. T4: Thyroxine. TPOAb: Antibodies against thyroid peroxidase. TGAb: Antibodies against thyroglobulin. Iron deficiency defined as serum ferritin level <12 ng/mL. **p value for comparison of iron deficiency and non-iron deficiency patients in the study group

Thyroid autoimmunity is the leading cause of thyroid dysfunction in iodine-sufficient countries (17). It has multi-factorial etiology and is considered to result from a combination of genetic and environmental factors, as well as nutritional determinants. Erdal et al. showed lower iron and selenium levels in 43 auto-immune thyroiditis patients than healthy controls (18). However, limited studies have investigated the relationship between iron status and thyroid auto-immunity through TPOAb and TGAb. Huet al. found that TPO activity, total T3 and T4 levels, and thyroid follicular volume were lower in iron deficiency rats than in those without iron deficiency (19). However, they did not evaluate TPOAb levels. Veltri et al. showed a cross-sectional study in 1900 pregnant women that iron deficiency was related with a higher prevalence of TPOAb and higher serum levels of TSH and lower free T4, independent of confounding factors including age and body mass index (20). Zhang et al. found in 1592 pregnant women that iron deficiency is a risk factor for increased TGAb, but not for TPOAb or subclinical hypothyroidism (21). Wang et al. demonstrated in 190 patients with TGAb or anti-thyroid microsomal antibody (TMAb) positivity that higher frequencies of hemoglobin and iron was observed in TGAb and TMAb positive patients than healthy subjects (22). They found anemia in 16.3% and iron deficiency in 14.2% of patients with positive anti-thyroid antibody titers. In accordance with these studies, we demonstrated decreased levels of hemoglobin, hematocrit, MCV, iron, ferritin, and transferrin saturation in patients with TPOAb and TGAb positivity compared to healthy individuals. We found higher prevalence of iron, ferritin, MCV, hemoglobin and transferrin saturation deficiency in patients with thyroid-specific antibodies. We also observed correlations between TPOAb and serum iron, ferritin, and transferrin saturation levels. Our results suggest that patients with thyroid-specific autoantibodies were at higher risk of development of iron deficiency and anemia. This may be due to the relationship between TPO activity and iron levels. It may indicate that low TPO activity resulting from low iron status causes an increase in thyroid autoimmunity with aim to maintain function. Low iron status may increase thyroid autoimmunity, as it could alter the binding of T3 to hepatic nuclear receptors and oxygen transport. Iron deficiency may also reduce the activity of other iron-containing enzymes, including myeloperoxidase and cytochrome oxidase, and therefore antibodies against these molecules could cause cross-reaction with TPOAb, leading to higher prevalence of thyroid autoimmunity (23). The relationship between thyroid autoimmunity and iron status may also result from the complex immunological etiopathogenesis of thyroid dysfunctions, in which common genetic and environmental factors play an important role. Besides, iron-deficiency anemia may be the first symptom leading to the diagnosis of subclinical hypothyroidism and thyroid autoimmune diseases. Patients with treatment-resistant anemia should be assessed for thyroid disorders. Autoimmune thyroid diseases should be considered in the differential diagnosis of anemia with unknown origin.

Several strengths of the present study are worthy of mention. Since inadequate intake of iodine could affect thyroid autoimmunity, we carried out the study in an iodine-sufficient area. There are many conditions in the etiology of iron deficiency anemia (24). We excluded conditions that might interfere with iron status, such as chronic inflammation, infections, drugs, pregnancy, smoking and obesity (25). In patients with autoimmune thyroid disease, the risk of iron deficiency may increase with concomitant autoimmune diseases including celiac disease, pernicious anemia, atrophic gastritis, SLE and rheumatoid disorders (4). We also excluded patients with these conditions from the study. Several limitations of the current work should also be mentioned. First, the study had a relatively small sample size. Second, to homogenize the study group, we conducted this study in only females. Thirdly, the study was limited to iodine-sufficient areas; thus, the results may not be generalized for women in iodine-deficient or iodine-excess

areas.

In conclusion, we found increased prevalence of iron deficiency in female patients with thyroid autoimmunity. Patients with autoimmune thyroid diseases were at higher risk of development of iron deficiency and anemia. We think that thyroid-specific antibodies should be investigated in patients with treatment-resistant iron deficiency anemia.

Conflict of interest

None to declare.

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The study protocol was approved by the Research Ethics Committee of Göztepe Training and Research Hospital, Medeniyet University (2015/0023).

References

1. Rayman MP. Multiple nutritional factors and thyroid disease, with particular reference to autoimmune thyroid disease. Proceedings of the Nutrition Society. 2019;78(1):34-44.
2. Ragusa F, Fallahi P, Elia G, Gonnella D, Paparo SR, Giusti C, et al. Hashimotos' thyroiditis: Epidemiology, pathogenesis, clinic and therapy. Best Practice & Research Clinical Endocrinology & Metabolism. 2019;33(6):101367.
3. Hu S, Rayman MP. Multiple nutritional factors and the risk of Hashimoto's thyroiditis. Thyroid. 2017;27(5):597-610.
4. Ruggeri R, Trimarchi F, Giuffrida G, Certo R, Cama E, Campennì A, et al. Autoimmune comorbidities in Hashimoto's thyroiditis: different patterns of association in adulthood and childhood/adolescence. Eur J Endocrinol. 2017;176(2):133-41.
5. Buzduga CM, Costea CF, Dumitrescu GF, Turliuc MD, Bogdănici CM, Cucu A, et al. Cytological, histopathological and immunological aspects of autoimmune thyroiditis: a review. Rom J Morphol Embryol. 2017;58(3):731-8.
6. Kawicka A, Regulska-Ilow B. Metabolic disorders and nutritional status in autoimmune thyroid diseases. Advances in Hygiene & Experimental Medicine/Postepy Higieny i Medycyny Doswiadczalnej. 2015;69.
7. Szczepanek-Parulska E, Hernik A, Ruchała M. Anemia in thyroid diseases. Pol Arch Intern Med. 2017;127(5):352-60.
8. Levi M, Simonetti M, Marconi E, Brignoli O, Cancian M, Masotti A, et al. Gender differences in determinants of iron-deficiency anemia: a population-based study conducted in four European countries. Annals of Hematology. 2019;98(7):1573-82.
9. Sherard GB 3rd, Newton ER. Is routine hemoglobin and hematocrit testing on admission to labor and delivery needed? Obstetrics and gynecology. 2001;98(6):1038-40.
10. Choi CW, Lee J, Park KH, Yoon SY, Choi IK, Oh SC, et al. Prevalence and characteristics of anemia in the elderly: cross-sectional study of three urban Korean population samples. American journal of hematology. 2004;77(1):26-30.
11. Cammack R, Wrigglesworth JM, Baum H. Iron-dependent enzymes in mammalian systems: CRC Press: Boca Raton; 1990.
12. Ashraf TS, De Sanctis V, Yassin M, Wagdy M, Soliman N. Chronic anemia and thyroid function. Acta Bio Medica: Atenei Parmensis. 2017;88(1):119.
13. Carvalho DP, Dupuy C. Thyroid hormone biosynthesis and release. Molecular and cellular endocrinology. 2017; 458:6-15.
14. Fayadat L, Niccoli-Sire P, Lanet J, Franc J-L. Role of heme in intracellular trafficking of thyroperoxidase and involvement of H2O2 generated at the apical surface of thyroid cells in autocatalytic covalent heme binding. Journal of Biological Chemistry. 1999;274(15):10533-8.
15. Maldonado-Araque C, Valdés S, Lago-Sampedro A, Lillo-Muñoz JA, Garcia-Fuentes E, Perez-Valero V, et al. Iron deficiency is associated with Hypothyroxinemia and Hypotriiodothyroninemia in the Spanish general adult population: Di@ bet. es study. Scientific reports. 2018;8(1):1-7.
16. Smith SM, Johnson PE, Lukaski HC. In vitro hepatic thyroid hormone deiodination in iron-deficient rats: effect of dietary fat. Life sciences. 1993;53(8):603-9.
17. Ranendra K, Sarada N. A Study on Anti Thyroid Peroxidase and Anti Thyroglobulin antibodies in patients with Thyroid Dysfunction. Journal of Dental and Medical Sciences 2020; 1(10): 14-18.
18. Erdal M, Sahin M, Hasimi A, Uckaya G, Kutlu M, Saglam K. Trace element levels in hashimoto thyroiditis patients with subclinical hypothyroidism. Biological trace element research. 2008;123(1-3):1.
19. Hu X, Teng X, Zheng H, Shan Z, Li J, Jin T, et al. Iron deficiency without anemia causes maternal hypothyroxinemia in pregnant rats. Nutrition research. 2014;34(7):604-12.
20. Veltri F, Decaillet S, Kleynen P, Grabczan L, Belhomme J, Rozenberg S, et al. Prevalence of thyroid autoimmunity and dysfunction in women with iron deficiency during early pregnancy: is it altered. Eur J Endocrinol. 2016;175(3):191-9.
21. Zhang Y, Huang X, Chen Z, Yang Q, Li X, Zhang R, et al. Iron deficıency, a rısk factor for thyroıd autoımmunıty durıng second trımester of pregnancy ın Chına. Endocrine Practice. 2020;26:(6). 595-603.
22. Wang Y-P, Lin H-P, Chen H-M, Kuo Y-S, Lang M-J, Sun A. Hemoglobin, iron, and vitamin B12 deficiencies and high blood homocysteine levels in patients with anti-thyroid autoantibodies. Journal of the Formosan Medical Association. 2014;113(3):155-60.
23. Haapala A, Hyöty H, Parkkonen P, Mustonen J, Soppi E. Antibody reactivity against thyroid peroxidase and myeloperoxidase in autoimmune thyroiditis and systemic vasculitis. Scandinavian journal of immunology. 1997;46(1):78-85.
24. Percy L, Mansour D, Fraser I. Iron deficiency and iron deficiency anaemia in women. Best practice & research Clinical obstetrics & gynaecology. 2017; 40:55-67.
25. Duntas LH. Environmental factors and thyroid autoimmunity. Annales d'endocrinologie; 2011; 72: (2) 108-13.