Objective: Microscopically, the thyroid gland is composed of spherical follicles and thyroid parenchyma includes two major cell types, the thyrocytes releasing thyroid hormones and C cells secreting mature calcitonin. Hypothyroidism has been known as being associated with the various abnormalities of the coagulation system. In the present study, it had been purposed to investigate the relationship between inflammatory hematological parameters, RBC, Hb, Htc, RDW, WBC, neutrophil, lymphocyte, N/L, Plt, MPV, PCT, PDW and hypothyroid hormonal status in the cases possessing the benign thyroid nodules.

Material and Methods: A total of 313 cases, 202 with hypothyroidism and 111 with euthyroidism possessing the benign thyroid nodules, that was verified with the cytological evaluation after one-endocrine surgeon performed ultrasonography (US) guided fine needle aspiration (FNA) (US-g-FNA), at the Division of Endocrine Surgery, Department of General Surgery, Giresun University Faculty of Medicine, Giresun, Turkey, in conformity with the criteria, were enrolled into the study during the period, from April 2010 to April 2015. The documents that were used to follow consisted of laboratory tests of the cases including both the thyroid hormones, free T3, Free T4, and TSH, and the inflammatory hematological parameters were reviewed and scanned retrospectively. The upper limit of the normal Thyrotropin (TSH) reference range was determined as 4 mU/L in the present study.

Results: No statistically significant difference was found between the inflammatory hematological parameters, RBC, Hb, Htc, RDW, WBC, neutrophil, lymphocyte, N/L, Plt, MPV, PCT, PDW, and hypothyroidism (p > 0.05).

Conclusion: Inflammatory hematological parameters may not be useful for estimating the hormonal status of the thyroid gland in the cases with the benign thyroid nodules verified with the cytological evaluation, TBSRTC.

Keywords: Thyroid neoplasms; Thyrocytes; Fine needle aspiration cytology (FNAC); Cytology; Thyrotropin (TSH); Hypothyroidism; Hematological parameters.

INTRODUCTION

The thyroid gland, weighing 10 to 20 grams in normal adults in the United States, is measured by ultrasonography (US) is a certain extent greater in men than women, increases with age and body weight, and decreases with increasing iodine intake (1, 2).

Microscopically, the thyroid is composed of the spherical follicles, each composed of a single layer of follicular cells surrounding a lumen filled with colloid (mostly thyroglobulin) and the thyroid parenchyma includes two major cell types, the thyrocytes releasing thyroid hormones and C cells secreting mature calcitonin (3). L-thyroxin (T4) and to a much lesser extent of l-triidothyronin (T3), two main thyroid hormones, are synthesized by the follicular epithelial cells, thyrocytes, of the thyroid gland (4).

Electron microscopy demonstrates the normal flat to low cuboidal follicular cells, interdigitating and overlapping one another. They are intimately relevant to the capillaries, surrounding the follicle; microvilli on the apical surface are multiplexed near the cellular
margins. When stimulated, the follicular cells become columnar and the lumen is depleted of colloid; when suppressed, become flat and colloid, accumulating in the lumen (5, 6).

The thyroid hormones frequently have a worthy effect on the erythropoiesis by enhancing it via hyperproliferation of the immature thyroid progenitors and increasing the secretion of erythropoietin (EPO) by resulting in EPO gene expression (7–10). The erythrocyte mass is increased in the most hyperthyroid status, whereas the hypothyroidism have an attenuated erythrocyte mass due to the reduction of plasma volume and may undetectable by routine measurement such as hemoglobin (Hb) concentration (11, 12). The thyroid dysfunction also changes the other hematological parameters, hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), white blood cell (WBC) count and platelet count (Plt). However, all the mentioned alterations return to normal if an euthyroid state is sustained (9).

In the present study, the laboratory tests of the patients having the benign thyroid nodules, verified with the cytological evaluation after one-endocrine surgeon performed ultrasonography (US) guided fine needle aspiration (FNA), had been evaluated retrospectively and purposed to investigate the relationship between the inflammatory hematological parameters, consisting red blood cell (RBC), Hb, Hct, red cell distribution width (RDW), WBC, neutrophil, lymphocyte, neutrophil lymphocyte ratio (N/L), Plt, mean platelet volume (MPV), plateletcrit (PCT), platelet distribution width (PDW), and the hypothyroidism.

MATERIALS AND METHODS

The present study had been conducted on a total of 313 cases, from April 2010 to April 2015 in order to matching two groups, the patients with hypothyroidism, 202 cases, and the patients with euthyroidism, 111 cases, control group. In terms of the inflammatory hematological parameters we measured RBC, Hb, Ht, RDW, WBC, neutrophil, lymphocyte, N/L, Plt, MPV, PCT, PDW. The five years documents consisted of laboratory tests of the cases included both the thyroid hormones and the inflammatory hematological parameters were reviewed and scanned retrospectively.

An elevated serum thyroid stimulating hormone (TSH) was determined as a TSH concentration above the upper limit of the normal reference range, typically accepted as 4 to 5 mU/L in the most laboratories. Presently a considerable controversy exist over the appropriate upper limit of normal for serum TSH that some authors have suggested that the true upper limit is only 2.5 or 3 mU/L in healthy individuals without any thyroid disease, whereas the others argue that the serum TSH distribution shifts towards higher values with age, independent of the presence of antithyroid antibodies (13), or in obesity. It is recommended for these cases that the normal upper limit could be as high as 6 to 8 mU/L in healthy octogenarians, or as high as 7.5 mU/L in morbid obesity (14). The upper limit of the normal TSH reference range was determined as 4 mU/L in the present study. Hypothyroidism has known as being associated with the various abnormalities of the coagulation system, such as the modification of coagulation proteins and bleeding tendency.

The study was performed for the cases which had been undergone US guided FNA (US-g-FNA) cytology (US-g-FNAC) and all the US-g-FNAC results had been reported according the guidance of The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), a 6-diagnostic-category system which was constituted through multidisciplinary formulation, proposed at the National Cancer Institute (NCI) Thyroid Fine Needle Aspiration State of the Art and Science Conference held in Bethesda, Maryland, 2007. TBSRTC is at present the most used and accepted reporting system for reporting FNA cytology (FNAC) worlwide (15). The use of TBSRTC also has been endorsed by 2015 American Thyroid Association (ATA) management guidelines (16) as 2009 ATA guidelines (17) which is a revision of 2006 ATA guidelines (18).

The criteria for including patients into the Study

The screening outcome revealed the 313 cases, 202 with hypothyroidism, 111 with euthyroidism, in conformity with the criteria, were incorporated into the study during the period, from April 2010 to April 2015. The exclusion criteria had been the hematologic disorders, cardiac disorders, autoimmune diseases, inflammatory or infective diseases, endocrinologic disease and diabetes, liver diseases, renal failure, recurrent diseases, thyroid malignancies and the previous or accompanying other malignancies, as well as those who had medical records as to the usage of steroids, anticoagulants, and alcohol along with those with a medical history of hepatitis and patients with the inappropriate samples.

Statistical Analysis

The statistical analyses were performed by using SPSS 23.0 computer program. Some descriptive statistics were calculated for control and hypothyroid groups. Some indexes of groups were compared by using Mann-Whitney U test due to the non-normality of the data sets.
RESULTS

111 (35.46%) out of 313 cases were possessing the euthyroid state, whereas 202 (64.54%) had the hypothyroid condition. It had not been detected any statistically significant difference between the cases with hypothyroidism, Group 1 and cases with the euthyroidism, Group 2, Control, in terms of the inflammatory hematological parameters, RBC, Hb, Htc, RDW, WBC, neutrophil, lymphocyte, N/L, Plt, MPV, PCT, PDW (p > 0.05) (Figure 1). Therefore, in accordance with the statistical test results, no any difference between the inflammatory hematological parameters and hypothyroidism was detected (Table 1).

DISCUSSION

Thyroid, a crucial endocrine organ, has a notable effect on the erythropoiesis by inducing EPO secretion and also the proliferation of erythroid progenitors (8, 11, 19). Hypothyrodism reported as cooccurrence with some coagulation system abnormalities, the most relevant.
vant one is expressed as acquired von Willebrand disease (20). The aim of the present study was to investigate whether any commitment between a kind of thyrocyte dysfunction, hypothyroidism, and inflammatory hematologic parameters, consisting RBC, Hb, Htc, RDW, WBC, neutrophil, lymphocyte, N/L, Plt, MPV, PCT, PDW.

Geetha and Srikrishna (21) reported RBC indices, comparing in the cases with hypothyroidism and hyperthyroidism and the study revealed that RDW and MCV in these groups in comparison to the euthyroid individuals had statistically significant difference. However, the other RBC parameters, such as Hb and Hct, did not exhibit any significant difference in comparison with the euthyroid hormonal status. Kawa et al (9) reported that RBC, Hb in the cases with hypothyroidism attenuated, while Hct was increased. They also showed that MCH, MCHC were lower and MCV was increased in hypothyroid group in comparison with the control group.

In the present study, the upper limit of the normal TSH reference range was determined as 4 mU/L and the comparison of the cases with hypothyroidism and the euthyroid ones had been performed for investigating the prediction of the current hormonal status of the thyroid gland by means of their inflammatory hematologic parameters. However, it was not detected any significant difference between the inflammatory hematologic parameters, RBC, Hb, Htc, RDW, WBC, neutrophil, lymphocyte, N/L, Plt, MPV, PCT, PDW and a type of thyroid hormone disturbance, hypothyroidism.

CONCLUSION

The present study investigated just hypothyroidism, performed on the cases that had benign thyroid nodular diseases in the duration of five years. The limitations of the present study may be the retrospective design, studying on the cases with the benign thyroid nodular diseases and not analyzing the thyroid antibodies, like antithyroid peroxidase Ab (anti-TPO Ab) or antithyroid microsomal Ab, antithyroglobulin antibody (anti-Tg Ab), and thyroid stimulating immunoglobulin (TSI Ab).

In conclusion, the usage of the inflammatory hematological parameters may not be beneficial for estimating the hypothyroid hormonal status of the thyroid gland in cases with the benign thyroid nodules that was verified with the cytological evaluation, TBSRTC.

DECLARATION OF INTEREST

No any conflict of interest relevant to this article has been declared.

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Abreviations

\( T_4 \) — L-thyroxin
\( T_3 \) — L-triidothyronin
EPO — Erythropoietin
MCV — Mean corpuscular volume
MCH — Mean corpuscular hemoglobin
US — Ultrasongraphy
FNA — Fine needle aspiration
US-g-FNA — US guided FNA
FNAC — FNA cytology
RDW — Red cell distribution width
PDW — Platelet distribution width
N/L — Neutrophil lymphocyte ratio
MPV — Mean platelet volume
Plt — Platelet
TSH — Thyroid stimulating hormone
TBSRTC — The Bethesda System for Reporting Thyroid Cytopathology
ATA — American Thyroid Association
anti-TPO Ab — Antithyroid peroxidase antibody
anti-Tg Ab — Antithyroglobulin antibody
TSI Ab — Thyroid stimulating immunoglobulin

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Sažetak

DA LI POSTOJI VEZA IZMEĐU TIPA TIREOCITNE DIFUNKCIJE, HIPOTIREOIDIZMA I ZAPALJENSKIH HEMATOLOŠKIH PARAMETARA U SLUČAJEVIMA SA BENIGNIM TIROIDNIM NODUSIMA?

5-GODIŠNJE ISKUSTVO JEDNOG CENTRA

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Uvod: Mikroskopski posmatrano, tireoidna žležda je sastavljena od sferičnih folikula i tireoidnog parenhima koji uključuje dva glavna ćelijaka tipa, tireociti koji oslobađaju hormone i C ćelije koje sekretuju zreli kalcitonin. Poznato je da je hipotireoidizam povezan sa mnogim abnormalnostima sistema za koagulaciju. U ovoj studiji, cilj je bio da se ispiša povezanost između hematoških parametara, RBC, Hb, Htc, RDW, WBC, neutrofila, limfocita, N/L, Pkt, MPV, PCT, PDW hipotireoidnog hormonskog statusa kod pacijenata sa benignim tireoidnim nodulima.

Materijal i metode: Ukupno 313 slučaja, 164 sa hipotireoidizmom, 111 sa eutireoidizmom i 38 sa benignim tireoidnim nodulima, koji su verifikovani citološkom evaluacijom nakon što je urađena ultrasonografija (US) vodećim tireoidnim nodulima koji su verifikovani citološkom evaluacijom, TBSRTC.

Rezultati: Nije pokazana statistički značajna razlika između inflamatornih hematoških parametara, RBC, Hb, Htc, RDW, WBC, neutrofila, limfocita, N/L, Pkt, MPV, PCT, PDW i hipotireoidizma (p > 0,05).

Zaključak: Inflamatorni hematoški parametri verovatno nisu dovoljno korisni za procenu hormonskog statusa tireoidne žležde u slučajevima sa benignim tireoidnim nodulima koji su verifikovani citološkom evaluacijom, TBSRTC.

Ključne reči: tireoidna neopazma, tireociti; aspiracija tankom iglom (FNAC); citologija; tireotropin (TSH); hipotireoidizam; hematoški parametri.

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