ORIGINAL ARTICLE

Association Between Thyroid Hormone Status and Complete Blood Count Parameters in Anemic Patients

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ABSTRACT

Introduction: Anemia and thyroid conditions effect each other in clinical practice. Anemia may induce alteration in thyroid hormone status and various thyroid conditions induce various types of anemia. In present study, we aimed to study the thyroid function tests of the anemic subjects and to compare characteristics and laboratory features of the three groups; hypothyroid, hyperthyroid, and euthyroid subjects. **Methods:** Anemic subjects divided into three groups according to the thyroid hormone status, either as hyperthyroid, hypothyroid and euthyroid groups. Hemogram indices and laboratory parameters compared between three groups. **Results:** Mean red cell distribution width (RDW) of hypothyroid anemic subjects was significantly lower than the RDW of euthyroid anemic subjects (p=0.003). White blood cell (WBC) count of hypothyroid anemic subjects was significantly reduced compared to the euthyroid (p<0.001) and hyperthyroid (p=0.047) anemic subjects. Significant inverse correlation between RDW and TSH (r=-0.25, p=0.001), between RDW and hemoglobin (r=-0.44, p<0.001), between RDW and hematocrit (r=-0.35, p<0.001) and between RDW and mean corpuscular volume (r=-0.53, p<0.001) were noted. **Conclusions:** Since anemia is common in thyroid conditions, besides its role in differential diagnosis of the anemia, RDW could also serve as an adjunct diagnostic tool in estimation of the thyroid hormone status in anemic subjects.

Keywords: Hypothyroidism, Hyperthyroidism, Anemia, Red cell distribution width, Leukocyte count

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INTRODUCTION

Anemia is a clinical condition of numerous underlying diseases. Besides many factors and disorders induce anemia, thyroid diseases are also associated with decreased hemoglobin (Hb) levels. For instance, hypothyroidism may cause microcytic, macrocytic, or normocytic anemia and moreover, it is not a rare initial finding in patients with hypothyroidism. As well as hypothyroidism, hyperthyroidism was also suggested to be associated with anemia (1, 2). It is well established that thyroid hormones, either directly or indirectly, interact with erythropoiesis in bone marrow.

Thyroid disorders do not only interfere with iron metabolism and cause iron deficiency, but also interact with serum cobalamin levels. In animal studies, hyperthyroidism was suggested to be associated with low cobalamin levels (3).

Anemia is a significant clinical finding that accompany to thyroid diseases. Both hypothyroid, hyperthyroid and euthyroid subjects with thyroid conditions may experience anemia. A study from In another study from Middle East in childbearing non pregnant women, it was reported that 44% of the women with abnormal thyroid function (subclinical hypothyroidism, hypothyroidism or hyperthyroidism) had anemia, and anemia was more common in this group compared to euthyroid women (4).

Although the rate of anemia in patients with thyroid diseases is well established, there is not much data about the thyroid status in anemic population in literature. Therefore, in present retrospective study, we aimed to study the thyroid function tests of the anemic subjects and to compare characteristics and laboratory features of the three groups; hypothyroid, hyperthyroid, and euthyroid subjects.

MATERIALS AND METHODS

Setting

The medical records of the patients that diagnosed with any type of anemia between August 2019 and February 2020 were analyzed right after approval from Ethics Committe of Abant Izzet Baysal University, No: 2018/290. Medical data were obtained from the database of the institution and from the patients' files. Subjects received treatment for anemia prior to the admission to our medical center, subjects received erythrocyte

transfusion within 6 months before admission, subjects with serious illness; such as advanced cancer, pregnant women and subjects under 18 years of age were excluded.

Participants

Study population was grouped into three according to the thyroid hormone status; hypothyroid, hyperthyroid and euthyroid groups. Age and sex of the participants as well as laboratory parameters, include thyroid stimulating hormone (TSH), free thyroxin (FT4), free triiodothyronine (FT3), hemogram indices (White blood cell [WBC] count, red blood cell count [RBC], hemoglobin [Hb], hematocrit [Htc], mean erythrocyte volume [MCV], erythrocyte distribution width [RDW], and platelet count [PLT]), serum iron, ferritin, transferrin saturation, vitamin B12 and folate levels, blood urea, creatinine, aspartate and alanine transaminases (AST, ALT), c-reactive protein, lactate dehydrogenase (LDH), total and indirect bilirubin levels were recorded for each participant. Data of the study groups were compared.

Statistical Analyses

Statistical analyses were done by using SPSS software (SPSS 15.0 for Windows, IBM Co., Chicago, IL). Distribution of the study variables in study groups were analyzed with Kolmogorov–Smirnov test. Categorical variables were compared in study groups by X^2 test and expressed as n, percentage. Kruskal-Wallis test was used in comparison of the variables without normal distribution and these data were expressed as median (interquartile range [IQR]). One Way ANOVA test was used in comparison of the variables with normal distribution and these data were expressed as mean ± standard deviation (SD). Tukey post hoc analyze was used to reveal the reason of statistical difference between study groups. Correlation between study variables were analyzed with Pearson's correlation test. Statistical significance was considered when the p value was lower than 0.05 level.

RESULTS

There were 173 subjects in the study; 124, 22 and 27 patients in euthyroid, hyperthyroid and hypothyroid groups, respectively. Mean ages of the euthyroid, hyperthyroid and hypothyroid groups were 48 ± 19, 53 ± 20 and 50 ± 10 years, respectively (p=0.44). 107 (86%) of 124 in euthyroid group were women and 17 (14%) were men, 16 (73%) of 22 in hyperthyroid group were women and 6 (27%) were men and 20 (74%) of 27 in hypothyroid group were women and 7 (26%) were men. Sex was not statistically different between study groups (p=0.13).

Both RBC (p=0.36), Hb (p=0.35), Htc (p=0.50), MCV (p=0.12), CRP (p=0.48), urea (p=0.13), creatinine (p=0.88), PLT (p=0.45), serum iron (p=0.38), total iron binding capacity (p=0.58), transferrin saturation (p=0.64), ferritin (p=0.33), vitamin B12 (p=0.33), folic acid (p=0.44), AST (p=0.52), ALT (p=0.46), LDH (p=0.69), total bilirubin (p=0.25) and indirect bilirubin (p=0.72) levels of the study groups were not statistically different. Table I summarized the general characteristics and laboratory data of the study population.

Table I: General characteristics and laboratory data of the study population

	Euthyroid group	Hyperthyroid group	Hypothyroid group	p
Gender				0.13
Women (n,%)	107 (86%)	16 (73%)	20 (74%)	
Men (n,%)	17 (14%)	6 (27%)	7 (26%)	
	Mean	*Standard Deviation*		
Age (years)	48 ± 19	53 ± 20	50 ± 10	0.44
TSH (uIU/mL)	1.49 ± 0.79	0.17 ± 0.15	10 ± 3.5	<0.001
FT3 (pg/mL)	1.1 ± 0.2	2.8 ± 1.1	0.6 ±0.2	0.001
FT4 (ng/dL)	1.21 ± 0.48	2.95 ± 0.9	0.91 ± 0.2	<0.001
RBC (M/mm^3)	4.17 ± 0.7	3.96 ± 0.8	4.1 ± 0.6	0.36
Hb (g/dL)	10 ± 1.5	9.8 ±1.2	10.3 ± 1.1	0.35
Htc (%)	33 ± 5	31 ± 3	32 ± 3	0.50
MCV (fL)	76 ± 11	78 ± 19	82 ± 17	0.12
RDW (%)	19.3 ± 3.4	18.5 ± 3.1	16.8 ± 4.1	0.004
CRP (mg/L)	1.5 ± 0.6	2.7 ± 0.1	2.3 ± 1	0.48
Urea (mg/dL)	28 ± 14	32 ± 13	34 ± 17	0.13
Creatinine (mg/dL)	1.34 ± 0.6	0.84 ± 0.3	0.9 ± 0.3	0.88
		Median (IQR)		
WBC (k/ mm^3)	6.4 (2.5)	6.4 (2.7)	5.03 (1.2)	<0.001
PLT (k/ mm^3)	288 (12)	303 (19)	276 (23)	0.45
Serum iron (µg/dL)	24.5 (2.8)	19 (2.9)	40 (2.5)	0.38
Total Iron binding Capacity (µg/dL)	406 (95)	420 (136)	360 (156)	0.58
Transferrin Saturation (%)	5.5 (1)	8.2 (1)	16 (2)	0.64
Ferritin (µg/L)	5.8 (3)	6.4 (4)	12 (3)	0.33
Vitamin B12 (ng/L)	294 (103)	239 (150)	338 (123)	0.33
Folic acid (µg/L)	6 (3)	5.6 (3.1)	6.6 (2.4)	0.44
AST (U/L)	17 (7.5)	16 (4.5)	16 (94)	0.52
ALT (U/L)	13 (10)	14 (5)	11 (9)	0.46
LDH (U/L)	157 (66)	150 (93)	202 (74)	0.69
Total bilirubin (mg/dL)	0.57 (0.4)	0.8 (0.3)	0.42 (0.3)	0.25
Indirect bilirubin (mg/dL)	0.3 (0.21)	0.3 (0.17)	0.34 (0.23)	0.72

Expectedly, TSH (p<0.001), FT3 (p=0.001) and FT4 (p<0.001) levels of the study groups were statistically different. Chronic comorbidities were present in 56 (45%) of euthyroid, 11 (50%) of hyperthyroid and 21 (78%) of hypothyroid subjects (p=0.01). However, chronic use of medications was present only in 14 (11%) of euthyroid, 4 (18%) of hyperthyroid and 7 (26%) of hypothyroid groups (p=0.13).

Mean RDW values of euthyroid, hyperthyroid and hypothyroid groups were 19.3 ± 3.4 years, 18.5 ± 3.1 years and 16.8 ± 4.1 years, respectively (p=0.004). In Post Hoc analysis, RDW of hypothyroid group was

significantly lower than the RDW of euthyroid group (p=0.003), however, it was not different from the RDW of hyperthyroid group (p=0.23). Post Hoc analysis was also revealed that RDW of euthyroid and hyperthyroid groups were not statistically different (p=0.55).

Median WBC values of euthyroid, hyperthyroid and hypothyroid groups were 6.4 (2.5) k/mm^3, 6.4 (2.7) k/mm^3, and 5.03 (1.2) k/mm^3, respectively (p<0.001). In post hoc analysis, median WBC of hypothyroid group was significantly lower than both the WBC values of the euthyroid (p<0.001) and hyperthyroid (p=0.047) groups, but, median WBC values of the hyperthyroid and euthyroid groups were not statistically different (p=0.61).

In Pearson correlation analyze, RDW was inversely and significantly correlated with TSH (r=-0.25, p=0.001), Hb (r=-0.44, p<0.001), Htc (r=-0.35, p<0.001) and MCV (r=-0.53, p<0.001) values (figure 1). WBC has not statistically significant correlation with any of the study parameters.

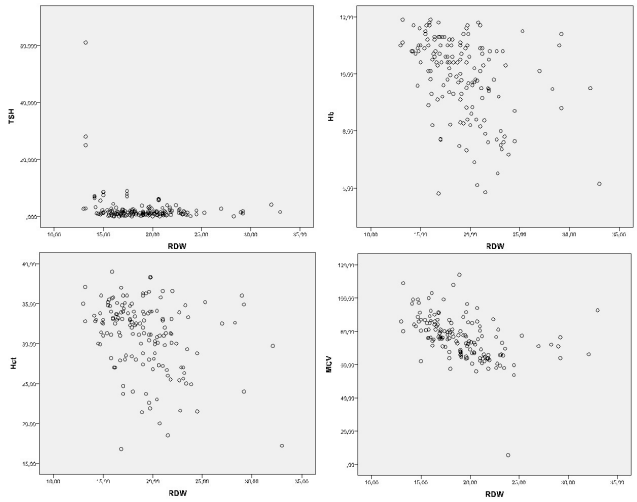

Figure 1: Correlations of RDW with TSH, Hb, Htc and MCV

DISCUSSION

In present study, we showed that anemic subjects with hypothyroidism have lower WBC values compared to the euthyroid anemic patients and to those with hyperthyroidism. Another important outcome of the study was reduced RDW levels in hypothyroid anemic subjects compared to the euthyroid anemic patients.

Thyroid disorders are associated with different kinds of anemia. About 38% of subjects with hyperthyroidism were shown to have anemia in a study from Germany (1). In present study, the most common cause of anemia among study population was also iron deficiency. Our results were also confirmed with previous studies in literature (5). It is not a surprising finding since iron deficiency is the most common cause of anemia in the world (6).

As a hemogram indice, RDW, is considered to be a marker of anisocytosis. Increased RDW reflect the production of erythrocytes in variable size. Moreover it has been suggested as a novel inflammatory marker in various clinical conditions (7-11). In animal model, hypothyroidism was shown to be associated with increased inflammatory cell infiltration in uterus (12). Moreover, Hashimoto's thyroiditis, an inflammatory condition of the thyroid, is usually associated with hypothyroidism in the late phase of the disease. Either hypothyroidism or hyperthyroidism are associated with oxidative stress and inflammation (13), therefore, significant inverse correlation between RDW and TSH in present study is not an unexpected outcome. Hyperthyroidism may increase the inflammatory burden by elevation of reactive oxygen species due to hypercatabolism and hypothyroidism may induce inflammation by reduced production of antioxidants (13).

We found that RDW was inversely correlated not only with TSH, but also with Hb, Htc and MCV values in anemic study population. Similarly, a study in literature showed that RDW was negatively correlated with Hb levels in any type of anemia (14). Since hematocrit is closely affected by Hb level, similar inverse correlation between RDW and Htc is also not surprising. MCV is the marker of erythrocyte size produced in bone marrow. Decreased MCV usually indicates iron deficiency anemia, which is associated with increased RDW. Therefore, an inverse correlation occur between MCV and RDW.

Decreased WBC count in hypothyroid group is an important finding of the present study. Authors found that lipid composition of the neutrophils, the most prevalent leukocyte of the peripheral blood, is rearranged in hypothyroid subjects (15). This reduction in lipid composition may result in a decrease in WBC count in hypothyroid subjects. Moreover, it has been reported that reduction in leukocyte count could be an unusual manifestation in patients with hypothyroidism (16). In an animal study, hypothyroidism was suggested to be associated with decreased WBC counts (17). The reduced WBC count in hypothyroid group in our study is consisted finding with literature.

Accompanying chronic diseases were more frequently present in hypothyroid group compared to hyperthyroid and euthyroid groups. Chronic anemia influence thyroid function and cause hypothyroidism (18). Moreover, hypothyroidism is prevalent in subjects with chronic kidney disease (19). Therefore, hypothyroid anemic subjects had more often accompanied chronic disease compared to euthyroid and hyperthyroid subjects in our study.

Relatively small study population and retrospective design are two limitations of present study. However,

significant negative correlation between TSH and RDW values in anemic subjects is a unique finding of our report.

CONCLUSION

Since anemia is common in thyroid conditions, besides its role in differential diagnosis of the anemia, RDW could also serve as an adjunct diagnostic tool in estimation of the thyroid hormone status in anemic subjects.

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