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Effect of Thyroid Dysfunction on Complete Blood Count

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ABSTRACT

Background: Thyroid hormones play a crucial role in metabolism and the proliferation of blood cells. Therefore, thyroid hormones have a direct effect on blood parameters by stimulating erythrocyte precursors and indirect effect by enhancing erythropoietin production. Additionally, it affects red blood cells include mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and red cell distribution width. In this study, we evaluated difference of complete blood count result between the healthy control, Hashimoto thyroiditis and Graves' disease study groups.

Methods and results: This is a cross-sectional study which included 158 subjects (male 9, female 149), categorized into three groups: control, hypothyroidism (patients with Hashimoto's thyroiditis), and hyperthyroidism (patient with Graves' disease).

The analyses showed a significant difference the between the groups in term of mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and red cell distribution width and monocyte (p values < 0.05).

Conclusion: The functional abnormalities of the thyroid gland significantly impact blood cells, and the complete blood cell count results play a critical role in the diagnosis of the condition.

1. Introduction

The one of the most significant endocrine gland in the human body is the thyroid gland. It secretes 3, 5, 3'-triiodothyronine (T3) and thyroxine which known as 3, 5, 3', 5'-tetraiodothyronine (T4). Dorgalaleh A et al reported,¹ these hormones have very important role in the body metabolism as well as early brain development, somatic growth, bone maturation, protein synthesis and regulating production of red blood cells.

Hormonal output from the thyroid is mediated by thyroid stimulating hormone (TSH) secreted by anterior pituitary. The secretion of TSH itself is mediated by thyrotropin-releasing hormone (TRH) secreted by the hypothalamus.

As R.S. Chandel et al have reported,^{2,3} thyroid hormones directly and indirectly stimulate erythrocytes precursors and enhance erythropoietin production, impacting blood parameters. Additionally, thyroid hormones promote erythropoiesis by stimulating hyper proliferation of immature erythroid progenitors and triggering the expression of the erythropoietin gene, leading to increased secretion of erythropoietin.

Hashimoto's thyroiditis (HT) and Graves' disease (GD) are primary thyroid gland disorders and leading causes of thyroid dysfunction (hypothyroidism and hyperthyroidism). Stephanie L Lee et al reported^{4,5}: The prevalence of HT is 0.3-1.5 cases per 1000 people and GD is 60-90% of all causes of thyrotoxicosis in different regions of the world. Hashimoto thyroiditis is characterized with lympho-monocytic inflammation of the thyroid gland and with an increase in serum levels of anti-thyroid peroxidase (anti-TPO) and/or anti-thyroglobulin (Anti-TG) auto-antibodies. Graves' disease is also an autoimmune disorder characterized by hyperthyroidism due to circulating autoantibodies (Anti-TSHR).

As Davaasuren.D et al have reported⁶: The First Central Hospital of Mongolia considered the diagnosis of 204 patients with thyroid disease from 2015 to 2017. Among these cases, thyroid nodules were 94 (46.1%), autoimmune thyroid diseases such as GD were 75 (36.8%) and HT were 27 (13.2%) and thyroid hyperplasia was 8 (3.9%). Moreover, Anti-thyroid stimulating hormone receptor (Anti-TSHR) in GD and Anti-thyroglobulin (Anti-TG) autoantibodies in Hashimoto's thyroiditis were increased, respectively.

As Montagnana et al have reported^{7,8,9}: Thyroid dysfunction such as hypothyroidism is generally associated with hypoplasia in all myeloid cell

lineages, whereas hyperthyroidism leads to hyperplasia. Consequently, thyroid disorders can have distinct effects on various blood cell lineages. Numerous studies reported changes in hematological parameters, including red blood cell (RBC), hemoglobin (HGB), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), white blood cell (WBC), and platelet (PLT) count, associated with thyroid dysfunction. These alterations have been observed in both hypothyroidism and hyperthyroidism. However, relation between thyroid hormones and complete blood count (CBC) measurements are limited in thyroid disorders.

In this study, we evaluate the effect of autoimmune thyroid diseases on the CBC and to investigate potential correlations of blood parameters and thyroid function abnormalities among Mongolian patients.

2. Materials and Methods

This cross-sectional study was conducted in Endocrine Outpatient Clinic of the First Central Hospital in Ulaanbaatar, Mongolia. The data were collected for two years between the periods from February 2015 to February 2017. In this study, we enrolled the patients with confirmed thyroid disorders by clinical manifestations, laboratory tests, and instrumental. The study's inclusion criteria involved participants who were voluntary completion of comprehensive laboratory and instrumental evaluation. On the other hand, exclusion criteria encompassed incomplete laboratory and instrumental tests, as well as patients with co-morbidities, blood disorders, and those who refused to participate. Ethical approval for the study acquired, and informed consent statements were obtained from all participants.

The hematological parameters examined by "SysmesXN2000" and consisted of WBC, RBC, HCT, HGB, MCV, MCH, red cell distribution with (RDW), and PLT counts. Thyroid hormone analysis (T3, free T4, TSH) was performed using radioimmunoassay and electrochemiluminescence methods. Thyroid specific antibodies including Anti-TPO, Anti-TG, Anti-TSHR, were assessed by fully automatic immunological analyzer "Cobas e411" in Roche, Germany, at the laboratories of FCH, UB-Songdo, and Mobio Hospital.

All statistical analysis was performed by STATA 14 software. Comparisons of parameters between two groups were performed using independent t-test and difference among multiple groups were analyzed using analysis of variance (ANOVA). A

value of $P < 0.05$ was considered statistically significant.

3. Results

The study included 158 patients with thyroid disorders (60 patients with HT, mean age \pm SD

(47.3 \pm 14.33) and 60 patients with GD, mean age \pm SD (39.05 \pm 13.46) and 38 healthy participants as control subjects, mean in age \pm SD (43.20 \pm 12.69). Among the study groups, majority of autoimmune disease cases (94.3%) were found in females (Table 1).

Table 1. Basic characteristics of study groups

Groups	Number of participants	Age (mean \pm SD)	Male (%)	Female (%)
HT	60	47.3 \pm 14.33	1.6 %	98.40 %
GD	60	39.05 \pm 13.46	10.50 %	89.50 %
Control	38	43.20 \pm 12.69	5.10 %	94.90 %
P value		0.42	0.06	

The table 2 represented that average TSH levels in HT (6.67 \pm 4.57 μ IU/ml) were statistically ($P < 0.001$) higher than both GD (0.05 \pm 0.12 μ IU/ml), and control groups (1.46 \pm 0.8 μ IU/ml). In the study groups, average level of Anti-TG and Anti-TPO in HT group (1130IU/L; 483.4 IU/ml) was significantly

higher than mean value of the control group (59.5IU/L; 44.1 IU/ml) and GD group (361.4IU/L; 254.7 IU/ml) respectively. A mean anti-TSHR level of 16.96 IU/L was observed in GD patients, which was higher than the other groups, but not statistically different.

Table 2. Comparisons of thyroid function tests

Groups	TSH (μ IU/ml) (mean \pm SD)	Anti-TG (IU/L) (mean \pm SD)	Anti-TPO (IU/ml) (mean \pm SD)	Anti-TSHR (IU/L) (mean \pm SD)
Control	1.46 \pm 0.8	59.5 \pm 124.6	44.1 \pm 168.1	0.3 \pm 0.1
HT	6.67 \pm 4.57	1130.5 \pm 1459.8	483.4 \pm 699.1	3.51 \pm 8.26
GD	0.05 \pm 0.12	361.4 \pm 691.4	254.7 \pm 239.6	16.96 \pm 13.7
P value	< 0.001	< 0.001	< 0.001	0.158

In table 3, the values of MCV, MCH, MCHC and RDW were statistically different between groups ($P < 0.05$). Interestingly, RDW levels were exhibited

from the reference range ($P < 0.001$) and positively associated with serum TSH levels ($P < 0.05$).

Table 3. Comparison of the red blood cell values between study and control group

Groups	Control group	HT group	GD group	P value
RBC	4.71 \pm 0.4	4.68 \pm 0.43	4.98 \pm 0.41	0.85
MCV	88.12 \pm 4.68	85.98 \pm 7.12	81.43 \pm 6.42	0.029
MCH	29.35 \pm 1.76	24.44 \pm 7.82	26.51 \pm 2.68	<0.001
MCHC	33.17 \pm 1.01	32.47 \pm 1.65	33.34 \pm 2.4	0.012
RDW-CV	13.44 \pm 1.33	20.08 \pm 12.2	13.37 \pm 3	<0.001
RDW-SD	41.20 \pm 5.48	39.40 \pm 8.89	39.68 \pm 2.97	<0.001
HGB	13.81 \pm 1.11	12.95 \pm 1.59	13.48 \pm 1.36	0.065

WBC values did not change in thyroid dysfunction but monocytes were statistically different between groups ($P < 0.05$). The mean values of PLT were

similar in different groups and were not statistically different (Table 4).

Table 4. Comparison of the white blood cell values and platelet count test between study and control group

Groups	Control group	HT group	GD group	P value
WBC	6.63 ± 1.44	6.53 ± 1.54	6.22 ± 1.83	0.158
NEUT	57.89 ± 7.66	55.31 ± 8.96	53.92 ± 10.67	0.143
LYM	33.21 ± 7.61	34.71 ± 8.47	35.63 ± 9.2	0.523
MONO	6.2 ± 1.95	7.02 ± 1.71	6.67 ± 3.51	<0.001
EOS	2.12 ± 1.19	2.23 ± 1.22	1.6 ± 1.39	0.593
BASO	0.59 ± 0.44	0.55 ± 0.35	0.35 ± 0.30	0.053
PLT	259.94 ± 34.62	279.98 ± 83.5	282.37 ± 75.35	0.301

4. Discussion

The most common laboratory thyroid hormonal tests such as T3, T4 and TSH play a vital role in assessing thyroid function and diagnosing hypothyroidism and hyperthyroidism. In addition to these, the most dependable indicators for HT and GD involve the detection of specific autoantibodies. The observation of higher TSH levels and autoantibodies levels in both Graves' disease and Hashimoto's thyroiditis patients compared to control group. This could be particularly relevant given the auto-immune nature of both conditions. Moreover, the impact of compounding factors, such as age, gender, and other comorbidities, warrants further investigation to enhance the accuracy of the findings^{10,11,12}.

CBC is indeed a widely used diagnostic method in routine medical practice. It provides valuable information about various components of the blood, including red blood cells, white blood cells, and platelets. This test is essential for detecting and monitoring anemia associated disorders, some side effects, including thyroid dysfunction.

L Horton et al¹³ and Omar et al¹⁴ reported, that HGB levels decreased in patients with hyperthyroidism. Additionally, in certain cases, mild anemia was observed among these individuals. Yeqing Gu et al also reported,¹⁵ thyroid hormones, including fT3, fT4 were positive association with HGB levels in euthyroid population. However, in our study group, there were no significant changes in blood platelet levels. This finding contrasted with another observation, wherein erythrocyte-derived anemia in thyroid disease was not significantly related to thyroid hormone levels in a Kenyan study¹⁶. The current studies indicated that reduction of red blood cell levels, including MCV, MCHC, MCHC, HGB occurred in patients with HT. Patients with GD exhibit elevated levels of RBC, while MCV, MCHC, NEUT, BASO were reduced compared to the control group. These results are consistent with several studies including Gilbert.H et al reported,^{17,18,19} indicating that relationship

between erythrocyte characteristics and thyroid dysfunction. Furthermore, CBC is a one of important laboratory test for diagnosing thyroid disorders.

The several measurements of blood composition were within the normal range except increased RDW levels in both patients with HT and GD in our study. Aktas G et al have also reported,^{7,20} similar findings. As Aktas G et al reported,²⁰ HT is characterized by inflammation of thyroid gland involving with lymphomonocytic cells. In this context, RDW has been associated to inflammatory diseases, leading researchers recommend its evaluation alongside other inflammatory markers in clinical practice. Moreover, Montagnana et al,⁷: MCV shows a positive correlation with serum TSH levels. This hypothesis suggests that premature aging of erythrocytes, increased RBC lipolytic potency in hyperthyroid patients, and alterations in erythrocyte membrane lipid distribution could contribute this association.

We observed positive correlation between RDW and serum TSH levels indicating that abnormal thyroid hormone levels may affect red blood cell size and RDW levels. Aktas G et al,²⁰ Guowei Zhou et al,²¹ Alexandra P.Bremner et al,²² and Khalid Abdelsamea et al reported,²³ these studies support our results indicating that abnormal thyroid hormone levels may affect red blood cell size and RDW levels. It has been observed in several studies^{20,21,22,23,24} that this hematological parameter is much higher than others, especially in hypothyroidism. On the other hand, Montagnana et al represented,⁷ positive correlations between MCV and serum TSH level. Same results presented in research of Samia Karkoutly et al²¹. Although L Horton et al¹³ and Nightingale et al²⁵ indicated, replacement therapy with thyroxine resulted in gradual decrease in MCV levels, even when the initial MCV value was within the normal range. That suggests a potential interplay between thyroid hormone levels and erythrocyte characteristics.

In the latest study of CBC changes in hypothyroidism suggested,²⁶ RDW and mean platelet volume (MPV)

levels could be novel predictors of inflammation in patients with hypothyroidism. They also revealed that MPV levels greater than 9.47 fL have 80% sensitivity and 72% specificity in predicting hypothyroidism, RDW levels greater than 13.4% have 80% sensitivity and 50% specificity in predicting hypothyroidism. Milosz et al demonstrated,²⁷ that thyroid hormones modulate cell production in the bone marrow by modify thyroid receptor gene expression and affect the proliferative potential of hematopoietic progenitor cells. Common association of elevated RDW with various health condition, such as anemias (iron deficiency, vitamin B12 deficiency, hemolytic), chronic inflammation, hemoglobinopathies, liver disease and heart failure, indicates variability in red blood cell sizes, prompting further investigation. Therefore, further studies are needed to elucidate this molecular mechanism, which will aid in diagnosis and treatment.

5. Conclusion

The red blood cell parameters, including RDW in patients with Hashimoto's thyroiditis and Graves'

disease were altered compared to healthy controls. General practitioners consider to the possibility of autoimmune thyroid disease when observing abnormal RBC values, especially RDW in routine blood tests. Further research is necessary to fully comprehend this relationship.

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Conflicts of Interest Statement

The authors have no conflicts of interest to declare.

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