ORIGINAL ARTICLE

Impact of Thyroid Dysfunction on Red Cell Indices in a Tertiary Care Hospital

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ABSTRACT

Background: The role of thyroid gland is to regulate the hematopoiesis in the bone marrow, which is carried out by inducing erythropoietin gene expression. The study aimed to compare red cell indices among different thyroid dysfunction disorders patients in our setup.

Methods: This retrospective observational study was conducted in Ziauddin University Hospital, Karachi in Clifton campus from January 2018 to September 2018. To maintain confidentiality, patient's identification was deleted. Total number of recruited patients was 485, out of which 117 were labeled as hyperthyroid, 169 were hypothyroid and 199 were euthyroid. Subjects for all three groups were between 20-60 years old. TSH level of patients were determined by VITROS® ECiQ immunoassay analyzer by Enhanced chemiluminescence technique. Data analysis was done on SPSS 20 while, mean and Standard deviation were calculated for quantitative variables. Percentages and frequencies were calculated for categorical variables and an independent t-test was applied to see significant differences among the groups.

Results: Comparison between hyperthyroid and hypothyroid groups revealed a statistically significant difference in the mean hemoglobin (p=0.036) and hematocrit (p=0.022). A statistically significant difference was also found in the RBC count (p=0.043) and hematocrit (p=0.032) while comparing hyperthyroid and euthyroid groups. There was no statistical difference between hypothyroid and euthyroid patients for any of the hematological parameters.

Conclusion: There was a proven association between thyroid dysfunction and erythropoiesis, which caused hematological indices to fluctuate, therefore hematological parameters, should be monitored in patients with thyroid diseases.

Keywords: Red Cell Indices; Erythropoiesis; Euthyroid; Hypothyroid; Hyperthyroid; Hematocrit; Mean Corpuscular Volume; Thyroid Stimulating Hormone.

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INTRODUCTION

The thyroid gland located in the neck, produces hormones that regulate metabolic rate and protein synthesis[1]. Thyroid hormones act on almost every cell in the body, thus thyroid hormones also regulate production of red blood cells. Patients with thyroid disorders often develop anemia. However, the precise mechanisms underlying this phenomenon remain largely unknown. The production of red blood cells (erythropoiesis) is a complex process that is strongly regulated by the body. Thyroid gland regulates many of the body functions mainly through secreting triiodothyronine (T3) and tetraiodothyronine (T4). These hormones influence nearly all the organ systems as well as growth and development. These effects are achieved mainly by the binding of active form of T3 i.e. free T3 to specific parts of nuclear receptor (TRA and TRB)[1,2]. T3 and T4 are synthesized and secreted via the follicular epithelial cells of thyroid gland and their secretion is regulated through Thyroid Stimulating Hormone (TSH), which is released from the anterior Pituitary gland[1].

One of the functions of thyroid hormones is its role in hematopoiesis in the bone marrow. During the differentiation from bone marrow stem cells to mature red blood cells, genes encoding proteins essential for mature red blood cells are switched on. Hyper production of immature erythroid precursors and increased secretion of erythropoietin (EPO) is caused by induction of erythropoietin genetic appearance. In addition, thyroid hormones can also enhance erythrocyte 2,3-Diphosphoglycerate, which increases the oxygen capacity, thus increasing its delivery to tissues[3]. Thus, there is a positive association between thyroid dysfunction and hematological parameters[3,4]. The prevalence of thyroid dysfunction is different in many societies, but hypothyroidism is the most prevalent one; its frequency being 2-5% cases annually[5,6]. In hypothyroidism, anemia is often seen and its prevalence is 20-60%[7,8]. There can be different types of anemia present in a hypothyroid patient, e.g. normocytic normochromic anemia; macrocytic and hypochromic anemia of moderate severity can be seen.

However, there can be hyperproliferation of immature erythroid progenitors as well[9]. As far as hyperthyroidism is concerned, anemia is not found in these patients, but erythrocytosis is common[4,10]. Once the state of euthyroidism is established, the hematological values return to normal[11]. When it comes to white blood cells and platelets, there is a decrease in total leucocyte (TLC) count as well as neutropenia and thrombocytopenia has been seen in hypothyroidism[12]. However, as compared to hyperthyroidism TLC is either, elevated, normal or slightly decreased and the number of neutrophils is relatively less. There is a definite hyperplasia of all myeloid cell lineages in hyperthyroism and hypoplasia in hypothyroidism[13]. Due to increasing trend in cases with thyroid dysfunction, the aim of this study was to evaluate the special effects of thyroid dysfunction on red cell indices in a tertiary care hospital in Karachi.

METHODS

This retrospective observational study was carried out at the Dr. Ziauddin Hospital Clifton Campus Karachi, from January 2018 to September 2018. Exemption was taken from institutions ethical review committee. Only data of patients with affirmed thyroid dysfunction were taken for this study. Patients with liver diseases and alcoholism were excluded which may become our confounders of the study. A total of 485 patient's data in which 117 patients were hyperthyroid, 169 patients were hypothyroid, and 199 patients were euthyroid was taken for comparison.

Initially TSH level of patients were determined by VITROS® ECiQ immunoassay analyzer by Enhanced chemiluminescence technique. Due to high sensitivity, wide dynamic range, and high signal-to-noise ratio, enhanced chemiluminescence is considered as one of the most popular detection methods for a variety of tests in clinical laboratory.

Reference range for thyroid stimulating hormone (TSH) is 0.36-4.94 µIU/mL in adults[14]. In concordance to this range, we divided patients into three groups; hypothyroid (TSH >4.94 µIU/mL), hyperthyroid (TSH<0.36 µIU/mL) and euthyroid (0.36-4.94 µIU/mL). Subjects for all three groups were from 20-60 years age group. We also retrieved the CBC results for these patients to review the hematological parameters and had drawn comparison among these groups.

Statistical analysis was done by using SPSS version 20 software and results were obtained by taking the Mean±standard deviation (SD) for measurable variables and percentages and frequencies for categorical variables. Independent t-test was used for substantial differences. p value of <0.05 was considered as a significant value.

RESULTS

A total of 485 subjects were included in the study. The age range of the subjects was 20-60 years. The subjects were categorized into three groups which included 24% hyperthyroid (n=117), 35% hypothyroid (n=169) and 41% euthyroid patients (n=199). The ratio of females in all groups was high as compared to males as shown in Table 1.

Table 1: General Characteristics of patient groups

Thyroid Status	n	Gender		Age	TSH
		Male n(%)	Female n(%)	Mean ± SD (Years)	Mean ± SD (mIU/ml)
Hyperthyroid	117	19 (16.2)	98(83.8)	37.47±10.41	0.13±0.11
Euthyroid	199	55(27.6)	144(72.4)	37.78±11.44	1.73±0.96
Hypothyroid	169	21(12.4)	148(87.6)	40.2±9.99	21.13±26.69

Comparison between hyperthyroid and hypothyroid groups revealed a statistically significant difference in the mean hemoglobin levels (p=0.036) and hematocrit (p=0.022) but no significant difference was found in the red blood count(RBC), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) as shown in Table 2. A statistically significant difference was found in the RBC count (p=0.043) and hematocrit (p=0.032) while comparing hyperthyroid and euthyroid but no significant difference was noted between patients in hyperthyroid and euthyroid for other hematological parameters including mean hemoglobin levels, MCV, MCH and MCHC as shown in Table 2. There was no statistical significance between hypothyroid and euthyroid patients for

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Table 2: Comparisons of Hematological Parameters in Different Thyroid Dysfunction Groups.

Thyroid Status (n)	Hb (g/dl)	RBC (x10 ^{12}/L)	Hct (%)	MCV (fl)	MCH (pg)	MCHC (g/dl)
Comparison between Hyperthyroid & Hypothyroid						
Hyperthyroid (117)	12.15 ±2.13	4.57±0.68	37.4±6.0	81.9±9.0	26.7±3.6	32.0±1.4
Hypothyroid (169)	12.68 ±2.10	4.67±0.65	39.1±6.2	83.6±8.8	27.3±3.4	32.1±1.2
p-value	0.036*	0.21	0.022*	0.104	0.223	0.788
Comparis on between Hyperthyroid & Euthyroid						
Hyperthyroid (117)	12.15±2.13	4.57±0.68	37.4±6.0	81.9±9.0	26.79±3.6	32.07±1.4
Euthyroid(199)	12.61±1.97	4.72±0.61	38.8±5.3	82.1±8.3	26.7±3.3	32.1±1.3
p-value	0.051	0.043*	0.032*	0.834	0.995	0.678
Comparison between Hypothyroid & Euthyroid						
Euthyroid(199)	12.61±1.97	4.72±0.61	38.8±5.3	82.1±8.3	26.7±3.3	32.1±1.3
Hypothyroid (169)	12.68±2.10	4.67±0.65	39.1±6.2	83.6±8.8	27.3±3.4	32.1±1.2
p-value	0.735	0.439	0.629	0.088	0.146	0.865

any of the hematological parameters as shown in Table 2.

Hemoglobin levels were highest in hypothyroid patients as compared to euthyroid and hyperthyroid groups as shown in Figure 1. Hematocrit was the only parameter that showed a statistically significant difference when comparing hyperthyroid and hypothyroid groups to each other and to the euthyroid group. The hypothyroid group has highest hematocrit as compared to hyperthyroid and euthyroid as shown in Figure 2. RBC count was the highest in the euthyroid group as compared to hypothyroid and hyperthyroid groups as shown in Figure 3.

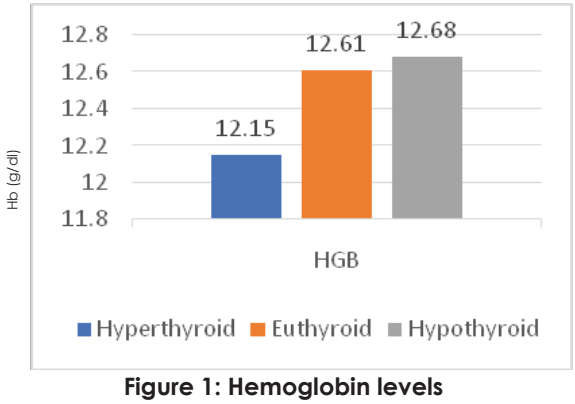

Figure 1: Hemoglobin levels

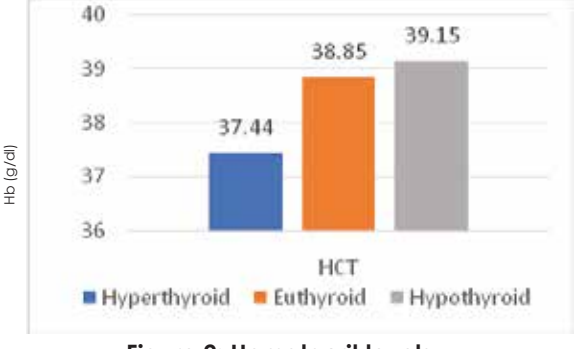

Figure 2: Hematocrit levels

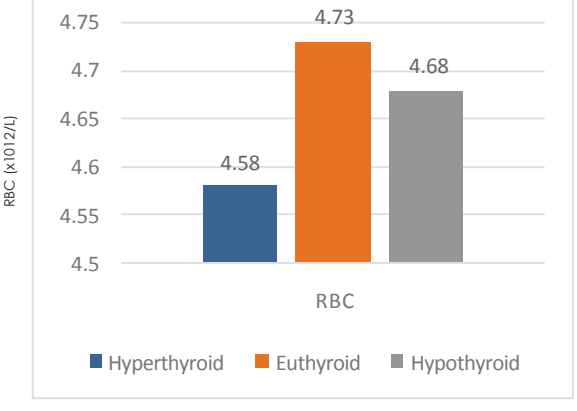

Figure 3: RBC Counts.

DISCUSSION

Thyroid hormones played important and crucial role in body metabolism and proliferation of hematopoietic cells. Thyroid dysfunction can lead to different effects on hematopoietic cells, which can cause anemia, erythrocytosis, leukopenia, thrombocytopenia and sometimes pancytopenia. Thus, in this study we attempted to evaluate effects of hypothyroidism and hyperthyroidism on RBC indices only. The data that we obtained showed that the values of Hb and HCT were statistically different between patients with hyperthyroidism and hypothyroidism ($p<0.05$), but RBC count, MCV, MCH and MCHC were not statistically different between these groups.

The RBC count and HCT were statistically different between euthyroid and hyperthyroid patients ($p<0.05$) whereas no statistical difference was seen in any of the parameters between patients with Hypothyroidism and Euthyroid. It is observed that not all hematological parameters like hematocrit, red cell count and hemoglobin are elevated in hyperthyroidism in spite of an increase in total red cell mass, which has been found in these patients due to simultaneous increase in plasma volume[16]. Erythropoietic variation and plasma volume modifications occur in those patients who experienced hyper functioning of thyroid so their hemoglobin levels could be normal, high, or low as is seen in our study which is not a surprising change.

In a study conducted by Dorgalaleh,[17] evaluating the effects of thyroid dysfunction on RBC indices, the results revealed that almost all the hematological indices (MCH, MCHC, HB, and HCT) except for RBCs ($p>0.05$) had a significant statistical difference ($p=0.0001$). Similar results were obtained for hyperthyroidism and hypothyroidism[17].

Another study reported the clinical relevance of thyroid dysfunction in human hematopoiesis by Kawa[2], portrayed that there was a statistically significant increase in HCT and MCV in hyperthyroid and hypothyroid patients, whereas compared to euthyroid group; there was an increase in the number of RBCs in hyperthyroidism and a significant decrease in the number of RBCs in hypothyroidism. In addition, there were similar changes in Hemoglobin values between hyperthyroidism and hypothyroidism[2]. In another study conducted in Saudi Arabia, red blood cell (RBC) count, hemoglobin and hematocrit value were significantly lower in thyroid disorders compared to euthyroid group and similar findings were seen in our study[18]. It was also found that the prevalence of anemia is higher in overt hyperthyroidism, which in accordance with our study[19].

A study by Bashir et al.[20] showed that there was a statistical difference in MCV values in patients with abnormal thyroid and that it was increased in both subclinical hypothyroidism and primary hypothyroidism[20-22]. While in our study, it was not increased in hypothyroid patients because there might be some constraints with current study like, limited data, and small sample size of hypothyroid patient (n=166) and we did not use high cut off for TSH i.e. more than 10 mIU/mL. TSH value more than 10 mIU/mL requires treatment and proper follow-up. Since this was a retrospective-hospital based study, which cannot be applied in our population so further large study trials are needed to see the role of all types of anemia and erythrocyte abnormalities in thyroid dysfunction patients in different tertiary care centers[23].

CONCLUSION

Thyroid dysfunction could fluctuate the effects on RBC indices. Therefore, we recommend routine screening for detection of thyroid disorders with hematological, biochemical and hormonal assay according to the American Endocrinologists Guidelines.

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CONFLICT OF INTEREST

There is no conflict of interest to be declared.

ETHICS APPROVAL

Ziauddin Faculty publications, discussed with academic authorities.

PATIENTS CONSENT

Retrospective data and patients identifications have been deleted.

AUTHORS' CONTRIBUTIONS

ES and SS designed the project, further ES and UA gathered the writing material and ES also done the data collection activity. AZ reviewed the manuscript while AA and SK performed the statistical analysis.

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