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Hematological Parameters in Euthyroid and Hypothyroid Females

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ABSTRACT

Introduction: Thyroid hormone is an important metabolic hormone affecting hematological parameters. A variation in the hematological picture is seen in patients with hypothyroidism.
Aims & Objectives: to study the differences in hematological parameters in hypothyroid and euthyroid females.
Place and Duration of Study: A Comparative Cross-sectional study using secondary data was conducted from February 2022 to March 2023 at Muhammad Medical College, Pakistan.
Material & Method: A total of 300 females (20-40 years of age, non-pregnant) were included in the study and based on their thyroid profile, they were divided into two groups, 160 with euthyroid status and another group of 140 with hypothyroidism. Hematological parameters were measured and compared in both groups. Data analysis was performed using Graph Pad Prism 9. A t-test, and one-way ANOVA were applied. The significance threshold is set at $P < 0.05$.
Results: A significantly increased TSH and decreased T3 and T4 ($p = < 0.05$) were estimated in hypothyroid females. The hematological parameters in hypothyroid females showed hemoglobin (11.18± 1.66), ESR (32.70± 19.84), MCV (77.02± 6.84), MCH (24.00± 3.03), MHC (26.99± 3.67) and RDW (18.03± 4.56). The difference in hematological parameters between euthyroid and hypothyroid groups was found to be statistically significant with a P value of <0.001.
Conclusion: Hypothyroidism showed a microcytic and hypochromic blood picture in females.

Keywords: Thyroid dysfunction, hypothyroidism, hematological parameters, blood composition, thyroid hormone.

INTRODUCTION

Thyroid hormones are one of the most important metabolic hormones in the human body. It is secreted from the thyroid gland. Triiodothyronine (T3) and thyroxin (T4) are two products of the thyroid gland. T4 is converted into T3 in the bloodstream by the deiodinase enzyme. T3 is the active form of thyroid hormone. T3 acts on its target organs either by intranuclear mechanism or intracytosol mechanism.[1] In the intra-nuclear mechanism, T3 binds to the intranuclear receptors. It stimulates the activation of target genes, while in the intracytosol mechanism, T3 binds to the receptors present in cytosol or mitochondria, and activates the molecular activation signaling cascade. This second mechanism is important for maintaining the BMR and cardiac cell metabolism.[2]

Thyroid hormones have a major and essential role in cell growth, division, differentiation, death, and metabolism. When the body develops a need for thyroid hormones, Thyrotropin cells in the hypothalamus secrete Thyrotropin-releasing hormones (TRH), which stimulate the release of thyroid-stimulating hormone (TSH) from the anterior pituitary, which activates the thyroid gland to release its hormones.[3] Hypothyroidism is a condition in which the thyroid gland fails to maintain the physiologically required amount of thyroid hormone (T3 and T4) in the blood, which stimulates the pituitary gland to increase the secretion of TSH in the blood. Therefore, in hypothyroidism, plasma levels of t3 and t4 decrease, whereas those of TSH increase.[4]

Hypothyroidism is divided into two categories based on the severity of clinical symptoms. One is overt, and the second is subclinical. Overt hypothyroidism is a condition in which the amount of free T4 in the blood is less than the reference range with elevated TSH, leading to the development of severe clinical symptoms. In subclinical conditions, the amount of free T3 and t4 is normal with elevated TSH. It does not lead to the development of clinical symptoms. [5]

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The clinical features of hypothyroidism are obesity, lack of ability to tolerate colds due to disruption of basal metabolism, loss of hairs, anxiety, depression, loss of reflexes, and constipation due to decrease of stimulation to axons of CNS and GIT.[6] The other features include clammy skin, swelling around the orbit of the eyeballs, and a deficit in the last portion of the eyebrows. [7]

Worldwide, the most reliable and efficient tests to evaluate the abnormal functioning of the thyroid gland are serum TSH levels and non-protein-bound free T4 levels in the blood. These two hormones are more sensitive to thyroid functioning than Triiodothyronine because Triiodothyronine is the hormone whose serum concentration gets affected by advanced thyroid dysfunction. [8]

Worldwide Primary hypothyroidism is more prevalent among females than men, with a peak age of 30 to 52 years. [9] The normal physiological range of TSH is 0.4 to 4.0 mU/L, and that of non-bound free T4 is 10 to 20 p mmol/L. [10] People who are at greater risk of having hypothyroidism are severely iodine deficient. The daily requirement of iodine in adults is 150 µg micrograms, and during pregnancy, it is 250 µg. [11] In a survey by the WHO, it was found that people in Pakistan have very severe iodine deficiency in their diets, which makes them more likely to develop hypothyroidism. Therefore, the estimated prevalence among the general population is 4.1%. [12] In many cases, hypothyroidism is associated with anemia, which can be defined as a reduced amount of hemoglobin or red blood cell count in plasma to maintain the physiological requirements of the body. [13] The World Health Organization gives the criteria for the diagnosis of anemia and more specifically the type of anemia. In females, the hemoglobin concentration is below 12 g/dl, and in males below 13 g/dl is considered to have anemia. MCV is the main indicator used to differentiate between types of anemia. In microcytic anemia, the MCV should be less than 80 fl, and in macrocytic anemia, the MCV should be more than 100 fl whereas in normocytic normochromic anemia, the MCV should be between the standard ranges of 80 fl to 100 ft in peripheral film or lab dings. [14] Many clinical studies worldwide found that the majority of patients suffering from hypothyroidism have lower serum levels of iron, vitamin B12, and folate, which not only affect RBC morphology but also suppress bone marrow function. Therefore, the common anemia encountered in hypothyroidism is iron deficiency anemia. [15]

Thyroid hormones have a crucial role in regulating hematopoiesis by stimulating the formation of hemoglobin in the adult population and regulating the maturation of hemoglobin in adolescents. Therefore, a deficiency of thyroid hormones causes hypoxia to develop in the body.[16] Hypothyroidism leads to a low ferritin level in the blood, decreased iron absorption from the GUT, and heaving menstrual bleeding, which leads to iron deficiency anemia. It can also develop macrocytic anemia due to a lack of absorption of vitamin B12 and B6 from the GUT mucosa, but this is reported very rarely.[17]

The current study is designed to study the hematological prospects of hypothyroidism.

MATERIAL AND METHODS

This Comparative Cross-sectional study was carried out from February 2022 to March 2023 at Muhammad Medical College and Hospital Mirpurkhas, with ethical approval later no MMC/292 dated 01-01-2022. Only non-pregnant women in the age range of 20 to 40 years were selected by convenience sampling technique. A total of 300 participants who were prescribed a thyroid profile by the consultants of OPD were selected and were divided into two groups: Group A 160 participants with euthyroid status and Group B 140 participants with hypothyroid status. All participants were provided with both verbal and written consent, which, after reading and understanding, they willingly submitted.

All the patients suffering from malignancy of the thyroid or any other disease were excluded from the study. 6 ml of blood was collected aseptically from the anticubital vein. 3 ml of blood was collected in an EDTA vial with anticoagulant and 3 ml in a clot activator vial without coagulant. Hemoglobin and RBC indices were estimated by an automated cell counter machine (B-C5150 Mindray). Anemia was considered with Hb less than 12 according to WHO criteria. Normocytic anemia was considered at 80 and 100 FL, microcytic anemia below 80 FL, and macrocytic anemia above 100Fl. The analysis of the clot activator vial was done using the Cobas 600 ECLIA Electrochemiluminescence method for the estimation of serum TSH. The hypothyroid status was considered at TSH >5.50 IU/ml and the euthyroid status was between 0.35 IU/ml and 5.5 IU/ml. The hyperthyroid status was at <0.35 IU/mL and they were excluded from the study.Data was collected on a purposely designed Performa.

Statistical analysis:

Statistical analysis was carried out by GraphPad Prism 9. The hematological indicators of euthyroidism and hypothyroidism were compared against each other. For continuous demographic

variables (e.g., age, BMI), one-way ANOVA was applied, and chi-square and Fischer exact tests were applied to obtain the P value, which was considered significant at a value less than 0.05.

RESULTS

A total of 300 patients were recruited for our study. The euthyroid group was comprised of 160 (53.4%) and the hypothyroid group was comprised of 140 participants (46.6%).

Table:1 Comparison of Age and BMI between Euthyroid and Hypothyroid Patients

Variable	Euthyroid patients n=160 Mean ±SD	Hypothyroid patients n=140 Mean ±SD	P value
Age of participants	27.36±4.51	25.16± 2.01	<0.001
BMI	19.47±1.52	26.60±3.52	<0.001

Table:1 examines the descriptive statistics of age and BMI of participants in euthyroid and hypothyroid patients. The prevalence of hypothyroidism was more common in younger females while the BMI of hypothyroid patients was increased indicating weight gain in hypothyroid patients. Statistical significance was noted at p-value < 0.001 by the student t-test.

Table 2: Hematological parameters in euthyroid versus hypothyroid patients

Variables	Euthyroid Mean ±SD	Hypothyroid Mean ±SD	*P value*
Hb	14.69± 1.85	11.18± 1.66	<0.001
ESR	15.88± 3.16	32.70± 19.84	<0.001
MCV	87.99±4.96	77.02±6.84	<0.001
MCH	29.85± 1.93	24.00± 3.03	<0.001
MCHC	34.25± 2.10	26.99± 3.67	<0.001
RDW	12.92± 1.19	18.03± 4.56	<0.001

*P value calculated using the one-way ANOVA showed a p-value less than 0.05.

Table 2 describes the difference in hematological parameters in euthyroid and hypothyroid patients. It was noted that in hypothyroid patients the hematological parameters were significantly lower. Statistically one-way Anova showed a value less than 0.05

Table 3: Serum level of TSH & T4 in Euthyroid versus Hypothyroid patients.

variables	Euthyroid Mean ± SD	Hypothyroid Mean ± SD	P value
TSH	2.25±1.06	5.97±2.06	<0.001
T4	14.37±2.87	8.93±3.01	<0.001

*P value calculated using the Fisher exact test showed a p-value less than 0.001

Table:3 examines the TSH in euthyroid (2.25±1.06) and hypothyroid (5.97±2.06) patients. It also describes the level of euthyroid (14.37±2.87) and hypothyroid (8.93±3.01). The P value was 0.001 expressing significance between the two groups.

DISCUSSION

The thyroid gland is responsible for maintaining basal metabolism, regulation of erythropoiesis, and maintenance of red blood cell membrane integrity. A deficiency of thyroid hormones badly inflicts the basal metabolic rate, making RBCs more prone to become victims of oxidative stress. The current study concludes that hypothyroidism leads to anemia. The type of anemia is microcytic and hypochromic. The values of Hb, MCV, MCH, MCHC, and RDW were found to decrease. The P value was 0.001. Research carried out throughout the world concludes that hypothyroidism is generally the most common cause of anemia, specifically microcytic hypochromic anemia. In 2022 Aparajita etal. concluded very similar results.[18] Because of decreased erythropoiesis, these is an increased fragility of RBCs cellular membrane leading decreased absorption of iron from the gastrointestinal tract. The current study also suggests that hypothyroidism also decreases total leucocyte count (TLC) and platelets. This result was also very similar to another study conducted by Meheshwari et al in 2020 which states that hypothyroidism not only affects red blood cell indices but also causes the development of deficiency of platelets (thrombocytopenia), deficiency of white blood cells (leukopenia) and deficiency of overall lineages of blood cells (pancytopenia).[19] Another study conveyed by Shetty

et al in 2018 also suggested similar results as the current study findings.[20] A study done by Mohammad et al in 2022 found similar findings to of current study.[21] A conflicting report was generated after the study by Arooj et al. in 2022 suggesting that only hemoglobin concentration decreased in patients of hypothyroidism but the other hematological parameters such as MCHC, MCV, and MCH remain unaffected.[22]

In 2023 Ganbattar et al reported that there is a direct relation between the values of TSH in blood with Red cell deviation width (RDW). An increase of RDW more than the value of 13% is 80% sensitive and nearly 50% specific predictor of hypothyroidism.[23] The serum level of TSH, T3, and T4 were found to decrease and this result is verified by a study conducted by Casis O in 2023.[24]

Patients with hypothyroidism have a variety of abnormalities affecting their white blood cells, platelets, and red blood cells that make up their hematological profile. These changes are a reflection of the intricate relationship between hematological activities and thyroid hormones. A thorough assessment of hematological markers is necessary for managing hypothyroidism and could aid in optimizing treatment plans to enhance patient outcomes. To clarify the underlying causes and therapeutic implications of hematological abnormalities in hypothyroidism, more research is necessary.

Limitations

There are certain limitations to this study. First, it was a cross-sectional study, Second, the sample size was small, Third, this study was conducted in one hospital, so the results cannot be applied to the whole population, and Fourthly, the presence of confounding variables.

CONCLUSION

This study concludes that hypothyroidism leads to microcytic and hypochromic anemia, with significant reductions in Hb, MCV, MCH, MCHC, and RDW (P = 0.0001) and decreases in TLC and platelet levels. These findings highlight the critical impact of thyroid dysfunction on hematological parameters. Regular hematological assessments are recommended for hypothyroid patients to improve treatment strategies and patient outcomes. Further research is essential to deepen our understanding and refine management approaches

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