

Comparison of Frequency and Types of Anemia in Subclinical Hypothyroidism and Euthyroidism

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ABSTRACT

Objective: To compare the frequency and types of anemia in subclinical hypothyroid and euthyroid patients.

Study Design: Comparative cross sectional study.

Place and Duration: Department of Medicine, PNS Shifa, Karachi Pakistan, from Jun 2019 to Dec 2019.

Methodology: All patients who fulfilled the inclusion criteria and visited Medicine Department, PNS Shifa Karachi were included in the study. After ethical approval and informed written consent patients were divided into two groups, subclinical hypothyroidism group (149 patients) and euthyroid group (148 patients). Blood samples of all included patients were sent for hematocrit, mean cell volume and hemoglobin level to assess the outcome i-e anemia & its different types.

Results: A total of 297 patients were included in the study. Amongst the sub clinically hypothyroid patients, anemia was noted in 40 patients (26.9%), while in the euthyroid group, it was noted in 23 patients (15.5%). In the subclinical hypothyroidism group, the type of anemia was microcytic in 13 patients (8.7%), macrocytic in 7 patients (4.7%) and normocytic in 20 patients (13.4%); while in the euthyroid group, anemia was microcytic in 7 patients (4.7%), macrocytic in 4 patients (2.7%) and normocytic in 12 patients (8.1%).

Conclusion: The commonest type of anemia found in sub clinically hypothyroid patients is normocytic normochromic anemia. The frequency of anemia was 26.9% in the subclinical hypothyroid group and 15.5% in the euthyroid group.

Keywords: Anemia, Euthyroid, Hypothyroidism.

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INTRODUCTION

Most cases of thyroid failure occur secondary to primary hypothyroidism with pathological processes of the thyroid gland accounting for 99.5% of the cases while the remaining 0.5% cases are secondary to a central pathology, i.e., Pituitary or hypothalamic abnormalities.¹ Patients having a raised serum thyrotropin or thyroid stimulating hormone (TSH) levels and a reduced serum free thyroxine (T4) levels are labelled as cases of overt primary hypothyroidism. Moreover, those having a raised serum TSH levels with a normal serum free T4 levels are labelled as cases of subclinical hypothyroidism.^{2,3}

Disorders of thyroid gland have a higher female preponderance with the disease more common amongst the women of child bearing age.⁴ The most prevalent thyroid gland abnormality across the globe is hypothyroidism with an estimated frequency of population affected being 2-5%. Subclinical hypothyroidism is commoner with a reported frequency of 4-12.8%.⁵ In addition to the above statistic, an estimated

2-5% patients progress from subclinical hypothyroidism to overt hypothyroidism per annum. The cutoff level of TSH requiring clinical evaluation and management in patients with overt or subclinical hypothyroidism is more than 10 mIU/L.⁶

A review of literature revealed an association of subclinical hypothyroidism with multiple pathologies including raised serum cholesterol level, atherosclerosis, infertility, neuropsychiatric disorders, coagulation disorders, and cholelithiasis.⁷ Hypothyroidism has been reported to cause different forms of anemia as well as hyper-proliferation of numerous immature precursor cells.⁸ The common reported types of anemia include normocytic and/or macrocytic hypochromic variants with an increased mean corpuscular volume (MCV) especially in patients with hypothyroidism of lesser severity.⁹

A research protocol by Erdogan *et al* published in 2012 from Turkey reported that the prevalence of anemia in the overt hypothyroid group was 43% while it was 39% in the subclinical hypothyroid group, and 26% in the euthyroid controls respectively. The difference between the overt hypothyroid groups and controls ($p=0.0003$) as well as the difference between subclinical hypothyroid groups and controls ($p=0.021$)

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were both statistically significant. However, the study reported a non-significant difference between the hypothyroid groups in terms of anemia.¹⁰

A large number of patients with overt and subclinical hypothyroidism present to medical outpatient departments, with a significant percentage also suffering from anemia. Our study intends to find a relationship between these two disorders in the local population. Keeping in view the magnitude of the problem and the limited number of studies available from Pakistan on this topic, this study was devised with the objective of this study comparing the frequency and types of anemia in subclinical hypothyroid and euthyroid patients.

METHODOLOGY

The comparative cross sectional study was conducted at the Medicine Department, PNS Shifa after taking permission from Hospital Ethical Review committee vide letter number ERC/2019/Med/34. The sample size was calculated by using the WHO sample size calculator by taking level of significance as 5%; absolute precision required=0.08; anticipated population proportion=26%.¹⁰ The sample size came out to be 297 patients. A total of 300 patients were enrolled in the study and divided into two equal groups consisting of 150 patients each but 3 patients were lost to follow up.

Inclusion Criteria: Patients aged 15 to 60 years, of either gender, having subclinical hypothyroid and euthyroid were included.

Exclusion Criteria: Patients with gastrointestinal or genitourinary system blood loss, prior history of thyroid medication, pregnancy, hemolytic anemias, comorbid diseases like renal insufficiency/ failure, coronary heart disease, uncontrolled hypertension, and diabetes mellitus were excluded.

The thyroid function tests comprising of serum TSH level, free T3 level and free T4 level were requested from the hospital laboratory using an Automated Analyzer and were diagnosed as subclinical hypothyroid and euthyroid patients. Patients were grouped into subclinical hypothyroidism group (Group A) and euthyroid group (Group B). After that, blood samples of all included patients were again sent for hematocrit, MCV and hemoglobin level, where blood analysis was done by a senior pathologist. The results were recorded on a predesigned performa.

Data analysis was carried out by using SPSS version 25. Mean and standard deviation were

calculated for numerical variables like age, hematocrit, hemoglobin, and MCV levels. Frequency and percentages were computed for qualitative variables like gender, presence of anemia, and type of anemia in subclinical and euthyroid patients. Chi square test was applied to compare qualitative variables while Independent sample t-test was applied to compare the numerical variables taking *p*-value ≤0.05 as significant.

RESULTS

A total of 297 patients were included in the study with 149 patients in the subclinical hypothyroidism group and 148 patients in the euthyroid group. In the subclinical hypothyroidism group, the mean age was 42.3±8.8 years, while in euthyroid group, the mean age was 41.8±9.6 years with the overall mean age of all patients included in the study being 42.0±9.2 years. In Group A, 38 patients (25.5%) were male and 111 patients (74.5%) were female, while in Group B, 32 patients (21.6%) were male and 116 patients (78.4%) were female.

The mean hematocrit level was 40.4±6.8% in Group A, while it was 43.8±5.5% in Group B respectively. The mean hemoglobin level was 11.1±1.9 g/dl in Group A, while in Group B, the mean hemoglobin level was 12.6±1.7 g/dl. Similarly, the mean MCV was 90.5±10.7 fl in Group A and 87.7±8.8 fl in Group B respectively. These results have been summarized in Table-I.

Table-I: Demographic and Laboratory Results (n=297)

Variable	Group A	Group B	<i>p</i> -value
Age (years)	42.3±8.8	41.8±9.6	0.676
Mean Hemoglobin (g/dl)	11.1±1.9	12.6±1.7	<0.001
MCV (fl)	90.5±10.7	87.7±8.8	0.015
Mean Hematocrit	40.4±6.8	43.8±5.5	<0.001

Table-II: Frequency and types of Anemia between the two Groups (n=297)

Variable	Group A n (%)	Group B n (%)	<i>p</i> -value
Anemia	40(26.9%)	23(15.5%)	0.017
Types of Anemia			
Normocytic	20(13.4%)	12(8.1%)	0.049
Macrocytic	7(4.7%)	7(4.7%)	
Microcytic	13(8.7%)	4(2.7%)	

In Group A, anemia was reported in 40 patients (26.9%), while in Group B, anemia was reported in 23 patients only (15.5%). Coming over to the types of anemia, in the subclinical hypothyroidism group, anemia was microcytic in 13 patients (8.7%), macrocytic in 7 patients (4.7%) and normocytic in 20

patients (13.4%); while in the euthyroid group, anemia was microcytic in 7 patients (4.7%), macrocytic in 4 patients (2.7%) and normocytic in 12 patients (8.1%). These results are summarized in Table-II.

DISCUSSION

Anemia is a serious public health concern in Pakistan, and conditions like hypothyroidism can further increase the number of patients as well as its severity.¹¹ In order to effectively treat an anemic patient correctly, the identification of correct diagnosis is necessary. Although the frequency of hypothyroidism varies between different countries, it is a fairly common disease. The prevalence of subclinical hypothyroidism in England was found to be 2.8% amongst males and 7.5% amongst females while it has been reported to affect 13.6% females and 9.2% males in the Pakistani population.¹¹⁻¹³ The disease is more prevalent in iodine deficient regions.^{13,14}

We found the prevalence of anemia to be 26.9% in the subclinical hypothyroidism group versus 15.5% in the euthyroid group, the difference being statistically significant ($p=0.017$). A study by Refaat *et al* reported that the frequency of anemia was 44% in the hypothyroid group versus 14.3% in the euthyroid group with the difference being statistically significant ($p<0.05$).¹⁵ The study also reported comparable results with regards to the various red blood cell indices such as hematocrit, MCV and hemoglobin levels.¹⁵

Anemia plays a role in the development of thyroxine deficiency (hypothyroidism) while hypothyroidism has been associated with development of anemia.¹⁶ Anand *et al* in 2017 reported that the frequency of anemia in patients with overt and subclinical hypothyroidism was 69% and 56% respectively ($p<0.05$). The commonest variety of anemia in patients with overt hypothyroidism (39%) and subclinical hypothyroidism (27%) was normocytic normochromic anemia, ($p=0.0125$), followed by microcytic hypochromic anemia reported in 20% and 18% patients amongst the respective groups ($p=0.618$). Macrocytic anemia was found to be less common with a frequency of 10% and 11% in overt hypothyroid and subclinical hypothyroid patients respectively ($p=0.75$).¹⁷

Another study by Kulkarni *et al* published in 2017 reported comparable results regarding mean hemoglobin levels with mean hemoglobin of 9.94 ± 2.03 g/dl in hypothyroid patients and mean hemoglobin level of 12 ± 2.19 g/dl in the euthyroid patients respectively ($p<0.0001$). Similarly, the study reported

comparable frequencies regarding types of anemia to our study. The frequency of anemia was 75% higher in the hypothyroid patients as compared to the euthyroid controls.¹⁸

Deficiency of thyroid hormones precipitates anemia by various mechanisms including stimulation of development of erythroid precursors, reduction in the levels of erythropoietin and a decreased supply of oxygen to the tissues.^{19,20} It is pertinent to find the exact cause of anemia as identification will guide the treatment plan. This study is the first of its kind examining the relation of subclinical hypothyroidism and anemia in the national literature. We found the most frequent cause to be normocytic normochromic anemia of chronic disease. It is recommended that work up for anemia should be carried out for all patients undergoing work up for thyroid disorders. Our study had a healthy sample size but we recommend more research protocols with larger number of patients to study the effect of thyroid hormone deficiency on anemia in the Pakistani population.

CONCLUSION

The frequency of anemia was found to be 26.93% in the sub clinical hypothyroid group and 15.48% in the euthyroid group. Normocytic normochromic anemia was found to be the most common variety of anemia in hypothyroid patients.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SJG & ZHM: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

WA & SFG: Data acquisition, data analysis, critical review, approval of the final version to be published.

KG & RB: Critical review, concept, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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