

## PREVALENCE OF ANEMIA IN PRIMARY HYPOTHYROIDISM PATIENTS

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### ABSTRACT

**Background:** Even though the association between primary hypothyroidism and anemia is commonly described, it is not known whether it is clinically relevant especially in subclinical hypothyroidism.

**Objectives:** In this study, we evaluate the prevalence of anemia and if present, etiology of anemia in patients with primary hypothyroidism. **Methods and patients:** 174 patients with clinical and laboratory signs of hypothyroidism presented to Endocrinology and Metabolic Diseases outpatient clinic of Tishreen University Hospital in Lattakia-Syria from January 2020 to January 2021. 85 patients with overt Hypothyroidism, 89 patients with subclinical Hypothyroidism were enrolled in this Study. All patients were subjected to full medical history, clinical examination, biochemical studies. Hypothyroidism was defined as TSH  $\geq 4.5$  mIU/L (subclinical [SHypo] with normal fT4 or overt [OHypo] with low fT4), Anemia was defined as Hb  $< 12$  g/dL in non-pregnant women and Hb  $< 13$  g/dL in men. **Results:** Anemia prevalence was 47.05% in the overt hypothyroid group, 13.48% in the subclinical hypothyroid group p-value=0.0001. Anemia of chronic disease was present in 30 patients (57.7%) followed by iron deficiency anemia in 20 patients (38.5%) and two patients (3.8%) had megaloblastic anemia with vitamin B12 deficiency. There was no difference between the hypothyroid groups in terms of anemia. **Conclusions:** The frequency of anemia in over hypothyroidism patients was high but Subclinical thyroid dysfunction was not an independent risk factor for developing anemia. Anemia of chronic disease is the most common type of anemia in hypothyroid patients, followed by iron deficiency anemia.

**KEYWORDS:** Subclinical hypothyroidism, Overt hypothyroidism Anemia.

### INTRODUCTION

Reduced production of thyroid hormone is the central feature of the clinical state termed hypothyroidism.<sup>[1]</sup> Primary hypothyroidism is the cause in approximately 99% of cases of hypothyroidism, with less than 1% being due to TSH deficiency or other causes.<sup>[2]</sup>

Autoimmunity is responsible for over 90% of non-iatrogenic hypothyroidism in countries with iodine sufficiency.<sup>[3]</sup>

Estimates of the incidence of hypothyroidism vary depending on the population studied. 2-5% of prevalence has been reported throughout the world. However, the prevalence of subclinical hypothyroidism is approximately 4-8.5%; it can reach to 20% in women aged 60 years or older.<sup>[4]</sup>

Hypothyroidism can affect all organ systems, and these manifestations are largely independent of the underlying disorder but are a function of the degree of hormone deficiency. Hematopoietic system is the primary one among these affected systems and prevalence of anemia in patients with hypothyroidism has been shown to be 20-60%.<sup>[5]</sup>

Anemia in hypothyroidism can be normochromic normocytic, hypochromic microcytic, and macrocytic. Anemia severity is associated with the hypothyroidism degree. Hypo cellular structure of the bone marrow gives rise to thought that thyroid hormones play a role in hematopoiesis. The most frequently encountered anemia type is normochromic normocytic anemia. The most frequent reason of this is the bone marrow repression due to thyroid hormone deficiency as well as lack of erythropoietin production arising from the reduction in need of O<sub>2</sub>. Erythrocyte life cycle in hypothyroidism is

normal, and there is hypo proliferative erythropoiesis. Thyroid hormones also increase 2-3 DPG (diphosphoglycerate) levels assisting in the transmission of oxygen into the tissues.<sup>[6]</sup>

Autoimmune thyroid disorders can be seen with other autoimmune disorders. Pernicious anemia can accompany hypothyroidism as a constituent of poly glandular autoimmune syndrome. Failure of vitamin B12 absorption occurs in pernicious anemia due to intrinsic factor (IF) deficiency and gastric achlorhydria. This is the reason of macrocytic anemia occurrence in hypothyroidism. Macrocytosis is found in 55% of the hypothyroid patients.<sup>[5]</sup>

Iron deficiency anemia is related with menorrhagia occurring as a result of various hormonal imbalances and also malabsorption which is seen in hypothyroidism.<sup>[7]</sup> Folic acid is another vitamin with impaired intestinal absorption, and causing macrocytic anemia in hypothyroidism.<sup>[8]</sup>

Indeed, relationships between thyroid disease and anemia have already been documented in experimental animal studies in the distant past but human data regarding relationships between thyroid disease and hematologic anomalies are scarce.<sup>[9]</sup>

Therefore, we aim to study the prevalence of anemia in hypothyroidism patients and to demonstrate the common type of anemia in overt and subclinical case.

### Patients and Methods

The study population was selected from patients who presented to the Endocrinology and Metabolic Diseases outpatient clinic of Tishreen University Hospital in Lattakia-Syria during a one year period (January 2020 to January 2021).

Exclusion criteria were multifactorial anemia or anemia due to other reasons including hemolytic anemias, gastrointestinal or genitourinary losses due to malignancy and/or acute/subacute blood losses from the respiratory, gastrointestinal, or genitourinary system; prior thyroid disorder and/or treatment history; presence of any comorbid disease like renal insufficiency/ failure, coronary heart disease, uncontrolled hypertension, diabetes mellitus, or any endocrine system disease other than hypothyroidism (subclinical, overt hypothyroidism); and patients who were under the treatment that might affect blood parameters such as steroids or who had received anemia treatment previously.

Thyroid function: TSH and free T4 concentrations were measured for all patients. Participants with a TSH level of 0.45 to 4.5 mIU/L were categorized as euthyroid. Overt hypothyroidism was defined as a TSH level .4.5 mIU/L in combination with reduced free T4 concentration. Subclinical hypothyroidism was defined

as a TSH level.4.5 mIU/L in combination with a normal free T4 concentration (0.82-1.63 ng/dl).<sup>[10]</sup>

Measurements of TSH, and FT4 were done with siemens immulite 1000 device.

Anemia: Anemia was defined according to the World Health Organization criteria (hemoglobin concentration, 130 g/L in men and, 120 g/L in women).<sup>[11]</sup>

Iron deficiency anemia is defined as ferritin levels lower than 10 ng/dL and with microcytosis and hypochromia in peripheral blood smear. Vitamin B12 deficiency anemia is defined as B12 levels lower than 189 pg/mL peripheral blood smear with increased MCV levels and with macrocytosis in Anemia of chronic disease is defined as defined as low Iron, low iron binding capacity and ferritin levels normal or elevated, and vitamin B12 levels normal.

### Statistical Analysis

Statistical analysis was performed by using IBM SPSS version20. Basic Descriptive statistics included means, standard deviations (SD), median, Frequency and percentages. Differences of distribution examined by using chi- square test or Fisher exact test if it need. Independent t student test was used to compare two independent groups. P value <0.05 was considered as statistically significant.

### RESULTS

210 patients with clinical and laboratory sighs of hypothyroidism presented to Endocrinology and Metabolic Diseases outpatient clinic from January 2020 to January 2021, 36 patients were excluded according to the exclusion criteria.

Of these 174 patients (89 patients had subclinical hypothyroidism and 85 patients had overt hypothyroidism). The median age of patients who enrolled in the study was 40.5 years, and 77.6% were female.

Demographic measures of Subclinical Hypothyroidism and Overt Hypothyroidism groups participating in this study are shown in Table 1.

**Table 1: Demographic characteristics of the study population.**

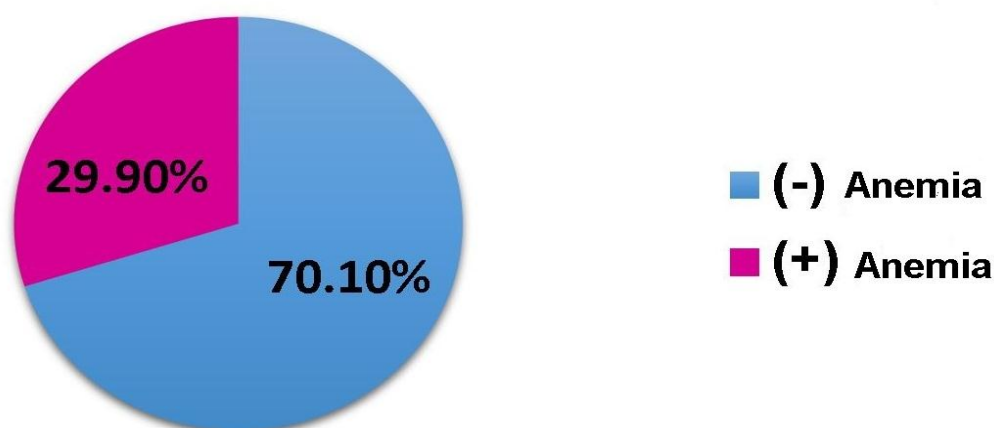
Variables	Overt Hypothyroidism (85 patients)	Subclinical Hypothyroidism (89 patients)	p-value
<b>Sex</b>			
Male	15(17.6%)	24(27%)	0.1
Female	70(82.4%)	65(73%)	
<b>Age(years)</b>	44.4±9.8	35.5±8.4	0.01
<b>age groups</b>			
20-30	10(11.8%)	16(18%)	0.02
30-40	22(25.9%)	36(40.4%)	
40-50	40(47.1%)	29(32.6%)	
50-60	13(15.3%)	8(9%)	
<b>Smoking</b>	37(43.5%)	30(33.7%)	0.1
<b>alcohol</b>	9(10.6%)	13(14.6%)	0.4

Biochemical values of Subclinical Hypothyroidism and Overt Hypothyroidism groups participating in this study are shown in Table 2.

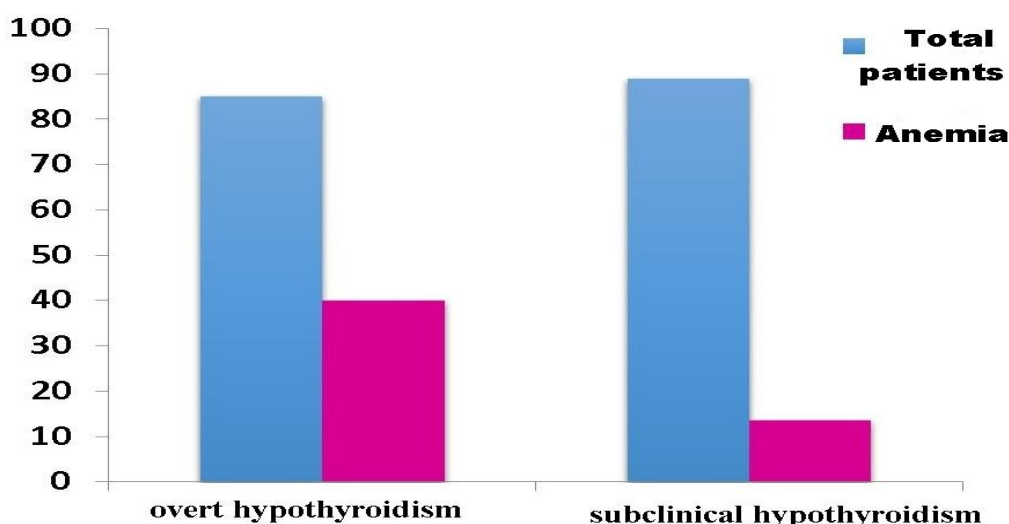
**Table 2: laboratory dates of the study population**

Variables	Overt Hypothyroidism (85 patients)	Subclinical Hypothyroidism (89 patients)	p-value
<b>TSH(mIU/mL)</b>	22.98±7.3	8.66±2.5	0.0001
<b>FT4(ng/dL)</b>	0.47±0.1	0.95±0.1	0.0001
<b>HGB(gr/dL)</b>	12.17±2.3	13.19±1.9	0.002
<b>CRP(mg/L)</b>	3.66±1.1	3±1.2	0.1
<b>MCV(fL)</b>	82.01±8.2	82.78±4.9	0.4
<b>Create(mg/dL)</b>	0.74±0.2	0.60±0.2	0.0001
<b>Ferritin(ng/mL)</b>	201.62±168.2	209.66±191.7	0.8

In our study; anemia frequency was 29.9% in the whole patients (Subclinical hypothyroidism and overt hypothyroidism) (Fig. 1).



Anemia was determined in 13.08% of those with subclinical hypothyroidism and 47.5% of those with overt hypothyroidism (Fig. 2). and the difference between these groups was statistically meaningful p-value=0.0001.



The etiologies of anemia in the all patients (Subclinical Hypothyroidism and Overt Hypothyroidism) are shown

in **Table 3**. Anemia of chronic disease frequency was found to be statistically meaningful ( $p=0.005$ ).

**Table 3: showing percent of various types of anemia with primary hypothyroidism**

etiology of anemia	Number of patients	percent
anemia of chronic disease	30	57.7%
iron deficiency	20	38.5%
vitamin B12 deficiency	2	3.8%

There was no statistical difference between the distributions of subclinical hypothyroid, overt

hypothyroid from Percentages of anemia reasons ( $p=0.2$ ). Table 4.

**Table 4: Percentages of anemia reasons in patients with anemia in all groups (Subclinical hypothyroidism, overt hypothyroidism).**

anemic patients (n:52)	Overt hypothyroidism (n:40)	Subclinical hypothyroidism (n:12)	P value
anemia of chronic disease	23(57.5%)	7(58.3%)	0.2
iron deficiency	15(37.5%)	5(41.7%)	
vitamin B12 deficiency	2(5%)	0(0%)	

## DISCUSSION

Although hypothyroidism frequency varies between countries it is a common disease. In the United States, 0.3% have overt hypothyroidism, and 4.3% have what has been described as subclinical hypothyroidism.<sup>[12]</sup> The risk of progression from subclinical to overt hypothyroidism is most closely related to the magnitude of serum thyrotropin [TSH] elevation and the presence of anti-thyroid peroxidase (TPO) antibodies. On the other hand, according to the data of WHO (World Health Organization), anemia is an important public health problem. In order to carry out the treatment of the patient with anemia correctly, it is necessary to determine etiological causes. The adverse effect of hypothyroidism on the hematological system can be anemia development. To the best of our knowledge there is no published study examining subclinical hypothyroidism and anemia in such a detailed content. In our study, we

examined this relationship of hypothyroidism (overt and subclinical) with anemia.

In our study, 77.6% of hypothyroid patients were female. Prevalence of anemia in overt hypothyroid and subclinical groups was 47.05% and 13.48% respectively. Thus, Anemia frequency in patients with overt hypothyroidism was found to be statistically significant when compared to subclinical hypothyroidism  $p$ -value=0.0001. Subclinical hypothyroidism was not an independent risk factor for developing anemia.

Also in our study, similar with the literature the most frequent anemia type was anemia of chronic disease 57.7%. The second most common type of anemia in our series is iron deficiency (38.5%) which is one of the most frequently seen diseases in all over the world. Iron deficiency anemia largely due to menorrhagia occurring

as a result of various hormonal instability and malabsorption observed in hypothyroidism.

Prevalence of vitamin B12 deficiency increases along with the age and the prevalence was observed as 1.6% to 10% in Europe.<sup>[13]</sup> In our study, vitamin B12 deficiency was 3.8 % similar with these values.

## CONCLUSION

we found an elevated anemia frequency in Hypothyroidism patients consistent with the literature, but prevalence of anemia in subclinical Hypothyroidism patients was not high like Overt Hypothyroidism patients. Anemia of chronic disease is the most common type of anemia in hypothyroidism.

It remains to be assessed in a randomized controlled trial whether treatment of hypothyroidism with levothyroxine is effective in reducing anemia.

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