Review Article

# Anaemia and hypothyroidism: a bidirectional relationship

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**Anaemia and hypothyroidism share a multifaceted relationship. This relationship extends from aetiology to management. Mineral deficiencies and autoimmunity can result in anaemia and hypothyroidism. Iron is essential for production of haemoproteins like haemoglobin and thyroid peroxidase. Hypothyroidism also causes anaemia by direct effects on erythropoiesis and increased blood loss. Hence, it can cause treatment refractory anaemia. These relationships affect management of both anaemia and hypothyroidism. Therefore, we should screen for anaemia in hypothyroidism and suspect hypothyroidism in treatment resistant anaemia.**

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Anaemia and hypothyroidism, though different diseases, have a lot in common. Both have a high prevalence in India. Both can be caused by a mineral deficiency; iron in the case of anaemia, iodine in the case of hypothyroidism. Thus, both are amenable to public health intervention by supplementation of the deficient mineral.

It is well known that anaemia is more common in hypothyroidism. In this article, we will review the bidirectional relationship between anaemia & hypothyroidism. We will explore causes of anaemia in hypothyroidism and its therapeutic implications.

## Epidemiology :

Hypothyroidism is common in India, with an estimated prevalence of 15.86% in adult females and 5.02% in adult males in urban areas[1]. It is of interest to note that Anti TPO antibodies were present in 21.85% of subjects. Anaemia is estimated to be present in 53.0% of adult females and 22.7% of adult males[2].

It has been observed that anaemia is more common in patients with thyroid disease. Anaemia was present in 5.9% of subjects in one study[3] while it was present in approximately 50% of subjects in another study[4]. Unfortunately, no such studies have been conducted in India. We can presume that we will have a higher prevalence due to the high prevalence of anaemia in the general population.

An Indian study[5] on anaemic hypothyroid individuals showed that normocytic normochromic type of anaemia was the most common type, seen in 51.6% of subjects. This was followed by microcytic hypochromic type in 43.3%. In 10% of subjects had megaloblastic anaemia, half of them because of pernicious anaemia. In another study[6] it was observed that hypothyroidism is the most common cause of macrocytosis without anaemia.

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- Anaemia and hypothyroidism share a multifaceted relationship.
- Hypothyroidism has direct effects on erythropoiesis, and increased blood loss causing treatment refractory anaemia.
- Screen for anaemia in hypothyroidism and hypothyroidism in refractory anaemia.
- Treat anaemia before giving L thyroxine if severe anaemia.

## Bidirectional Relationship :

It has long been observed that thyroid disorders increase risk of anaemia[7]. The enzyme, thyroid peroxidase, which catalyses thyroid hormone production is a haemoprotein[7]. Also, there are other mechanisms which form the complex, bidirectional relationship between anaemia & hypothyroidism. They are discussed below.

## Direct Effects :

Thyroid hormone plays an important role in haematopoiesis. They cause proliferation of erythrocyte precursors and stimulate erythropoietin production[8]. In hypothyroidism, reduced number and proliferation of erythrocyte precursors is observed in the bone marrow. Also, levels of erythropoietin are lower in hypothyroid individuals. This affects treatment of anaemia. Some of this reduction is due to a lower basal metabolic rate and lesser oxygen demand. Reduced erythropoiesis results in a normocytic normochromic type of anaemia.

Hypothyroidism is a hypocoagulable state. Reduced levels of von Willebrand factor have been observed in some patients with hypothyroidism[9]. Females in the reproductive age group experience increased menstrual bleeding due to hypothyroidism[7]. It has a multifactorial etiology. TSH shares its alpha subunit with LH and FSH. This leads to a reduction in LH secretion resulting in reduced progesterone levels. Also, there is reduced sex hormone binding

globulin production resulting in increased free estrogen levels which manifest as increased menstrual bleeding.7 Increased blood loss manifests as microcytic hypochromic anaemia.

## Autoimmunity — A Connecting Link :

Hashimoto's disease is the most common cause of hypothyroidism in iodine replete populations[1]. It is an autoimmune disease. An association with other autoimmune diseases like coeliac disease, autoimmune haemolytic anaemias and atrophic gastritis has been observed[7].

Coeliac disease[10], pernicious anaemia and atrophic gastritis[11] affect absorption of vitamin B12. Vitamin B12 deficiency was observed in a study on anaemic hypothyroid individuals[5]. However, folate deficiency was not seen in that study. They manifest as megaloblastic anaemia. Macrocytes are observed in the peripheral blood while megaloblasts can be seen in the bone marrow. They may also lead to Iron malabsorption which leads to microcytic, hypochromic anaemia.

Autoimmune haemolytic anaemias have been reported in association with autoimmune thyroiditis[7]. They present with normocytic, normochromic anaemia along with presence of abnormal RBCs on a peripheral blood smear.

Anaemia may be the first presenting feature of many autoimmune rheumatic disorders[12]. They are more prevalent in patients with thyroid disorders.

## The Role of Minerals :

As thyroid peroxidase is a haemoprotein, iron is essential for its function. Hence, Iron status affects thyroid function[13]. Iron supplementation has been reported to improve thyroid status in patients with subclinical hypothyroidism[14].

## Iatrogenic Effects :

It has been reported that oral intake of Iron salts may reduce absorption of levothyroxine resulting in higher dose requirements[15].

Also, anaemia can reduce acceptability of levothyroxine by increasing risk of adverse effects like tachycardia, anxiety and restlessness. Hence, it is recommended that moderate to severe anaemia be corrected before starting levothyroxine[16].

## Therapeutic Implications :

Anaemia and hypothyroidism are highly prevalent in India. Therefore, it is likely that both might be present in the same individual. This complicates aspects of management which have been mentioned in Table 1.

For patients with anaemia, we should be thyrovigilant as thyroid disorders may cause anaemia. They may also affect response to treatment. In uncomplicated nutritional iron deficiency, erythropoietin levels are high. Hence, there is a rapid response to iron supplementation. In case of hypothyroid patients, since erythropoietin levels are lower, there may be reduced response.

Table 1 — *Management of anaemia in hypothyroidism*

| Morphological subtype | Probable Causes | Remarks |
|---|---|---|
| MCV Normal Normocytic Normochromic type | • Direct effect of ↓ T3 on bone marrow, erythropoietin production<br>• Associated autoimmune haemolytic anaemia<br>• Early stages of Iron deficiency | • Treat hypothyroidism; Anaemiay will correct automaticall<br>• Look for abnormal RBC on PBS → evidence of haemolysis |
| MCV Low Microcytic Hypochromic type | Iron deficiency<br>• ↑ bleeding<br>• ↓ absorption | • Supplement Iron + treat hypothyroidism<br>• Treat both together even if subclinical hypothyroidism.<br>• Treat anaemia before giving L thyroxine if severe anaemia |
| MCV High Macrocytic type | Vitamin B12 deficiency<br>• ↓ absorption | Look for pernicious anaemia, coeliac disease and atrophic gastritis |

So, patients with anaemia, especially those refractory to treatment should be screened for thyroid disorders.

Similarly, practicing rubrivigilance for anaemia in hypothyroidism would be helpful. Anaemia is a common manifestation of hypothyroidism. Iron deficiency adversely affects thyroid function. Also, both anaemia and hypothyroidism can present with a subjective feeling of weakness. Therefore, their clinical presentation overlap. Hence, management of hypothyroidism should include screening for anaemia.

Unfortunately, despite their prevalence, there is a lack of Indian studies on anaemia in hypothyroidism. We hope this article will lead to more research and better management of anaemia and hypothyroidism.

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