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# Normal anemia caused by endocrine disease: Case study from Jordan

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***Abstract*---**Anemia is a common condition in patients with thyroid disorders. This paper focuses on demonstrating that changes in hemoglobin concentration, hematocrit, red blood cell count and erythrocyte indices influence the development of this pathology. The reduced half-life and decreased erythropoietin production of red blood cells and proliferation of blood cell precursors in the bone marrow made it possible to establish a relationship between the patient's symptoms and the prevailing laboratory findings between anemia and hypothyroidism.

***Keywords*---**Anemia, Thyroid Disorders, Hemoglobin, Hematocrit, Red Blood.

## Introduction

Micronutrient deficiencies can hamper human growth and development. The risk of deficiencies of different micronutrients (micronutrients) can occur simultaneously because the diet tends to be monotonous and/or the available and consumed food sources are of low nutrient density (Hess, 2010). Anemia and iodine deficiency are general nutritional problems; the invisible but detrimental effect of HR preparation is the occurrence of cognitive developmental disorders that will eventually lead to intellectual lowering (Ashraf et al., 2017).

Anemia is a condition in which the number of red blood cells is insufficient to meet the physiological needs of the body. At the population level, anemia is measured based on hemoglobin levels, which are always related to the sufficiency of iron, one of the constituent elements. Anemia can also occur due to a number of reasons, but the most important factor is iron deficiency. About 50 percent of anemia cases are considered to be due to iron deficiency, but the percentage varies depending on regional circumstances. Other causes of anemia are deficiency of folic acid, riboflavin, vitamins A, B12, acute and chronic infections (such as malaria, cancer, tuberculosis, HIV), and congenital or acquired disorders

that affect hemoglobin synthesis, red blood cell production, or red blood cell survival (such as hemoglobinopathy) (WHO, 2011; 2015).

Because of iron deficiency, the prevalence of anemia is an important indicator of health and hemoglobin concentration can provide information about the severity of iron deficiency. In the absence of chronic disease or hemoglobinopathy. 8 Aside from being an important determinant of anemia, studies in recent decades have shown that iron deficiency can also lead to decreased levels of intracellular enzymes that require iron and are involved in many metabolic pathways. With or without anemia it will interfere with thyroid hormone metabolism. When compared with those with adequate iron, T3 levels were 10 percent lower in those with moderate to severe iron deficiency anemia and iron deficiency without anemia.

The global prevalence of anemia in the general population is 24.8%, indicating that approximately 1.620 million people develop it annually (Khanam & Khan, 2021). In fact, anemia affects key sectors, especially the most vulnerable groups such as children aged 0-5 years, and they account for 25.7% of anemia cases (De Benoist et al., 2008).

A hemoglobin range of less than 14 g/dL in men, and 12 g/dL in women (Lim et al., 2020) is identified as anemia. This disease is caused by a deficiency of one or more essential nutrients in the body, such as iron, folic acid, and cobalamin, which are disorders that affect hemoglobin production and are linked to some chronic diseases (Elstrott et al., 2020). Chronic disease anemia is a condition that accompanies a specific underlying disease, generally initiated by cellular immune mechanisms, proinflammatory cytokines, and hepcidin. It is the second most common type of anemia after iron deficiency anemia in the world (Lee, 2020).

A physical exam can provide useful information for diagnosing the cause of anemia. It is important to make changes in the skin, mucous membrane, lymph nodes, respiratory system, cardiovascular system, urinary system, endocrine system, nervous system and everything related to the clinical picture of the patient. A complete blood count allows the presence of anemia to be shown and provides information about its severity and possible causes to guide the correct diagnosis. They are generally classified by hematological indices, which will help us characterize and identify the pathological origin (Dobay et al., 2017). The development of this paper aims to perform the analysis of the hematological values of the anemic patient, by reviewing the bibliographic sources to resolve the clinical case raised, the importance of which lies in knowing the contribution from the clinical point of view. To display the elements provided by blood biometrics, to facilitate the identification of the etiology of the patient and the subsequent improvement of the state of health. However, this paper focuses on the interpretation of the hematological values of an anemic patient, by reviewing bibliographic sources to resolve the clinical case.

**Anemia**

It is characterized as a hemoglobin value of less than 14 g / dL in male patients and 12 g / dL in female patients, in infants it will vary by age, as defined by the

World Health Organization. This can happen for various reasons, the most common being nutrient deficiencies, chronic processes and diseases that affect hemoglobin (Shubham et al., 2020). Anemia types in the pathophysiological classification, the value of the normal reticulocyte count from 0.5 to 1.8% will be taken into account, if these are increased it will be regenerative anemia and if they are reduced it will be antigenic (Buttarello, 2016). It would be classified according to erythrocyte morphology (MCV < 80fl), normal (MCV 80-100 fl) and microcytic (MCV > 100 fl) (Buttarello, 2016).

**Normal Anemia**

These are those whose red blood cells range in size from 80 to 100 fl. They can be classified according to the response of retinal cells whose normal value ranges from 0.5 to 1.8% (Buttarello, 2016). High reticulocyte regenerations occur in severe hemorrhagic and hemolytic anemia, while normal or reduced reticulocyte regenerations in the absence of other leukopenia are caused by infectious or inflammatory diseases or drug side effects; On the other hand, when associated with other leukopenia, it is associated with lymphadenopathy or splenomegaly (Khanam & Khan, 2021). In patients with impaired thyroid function, cases of anemia usually occur frequently due to triiodothyronine deficiency, which results in defective erythrocyte maturation. Cobalamin and folic acid deficiencies are usually associated with cases of hyperthyroidism (Dubaj et al., 2020).

**Laboratory Tests**

The initial laboratory evaluation of patients with anemia should include basic criteria including:
Hematocrit: The percentage of the surface volume of red blood cells in relation to the blood. Its normal value in the male population is 40.7% and the female population is 36.1% (Lim et al., 2020). Elevation is the result of some diseases such as anemia, hemolysis, mononucleosis, and nutritional deficiencies. It may be increased in congenital heart conditions, low plasma oxygen levels, and scarring or in patients with spinal cord disorders ((Handin et al., 2003; Pasternak et al., 2008; Paller & Mancini, 2015).

Hemoglobin: is a hemoprotein of vital importance for its concentration because it is responsible for transporting oxygen. Its standard value is 13-16 g/dL in female patients and 14-17 g/dL in males (Pischik, 2006; Dobay et al., 2017). High levels can be an indication of polycythemia. This can lead to blood clots and heart attacks. Low levels generally indicate that you have some form of anemia (Dameshek, 1950; Sueters & Oepkes, 2014).

**Red blood cells:** help diagnose different types of blood disorders. Their normal values: 4.7 million (mcL) in men and 4.2 million (mcL) in women (Dobay et al., 2017). Its higher concentration is associated with kidney tumor, hypoxia in the circulatory system, and bone marrow damage. A low value indicates anemia, bleeding, bone marrow failure, erythropoietin deficiency, hemolysis due to transfusion, vascular injury, iron, folic acid, pyridoxine, and cobalamin deficiency (Sueters & Oepkes, 2014; Dobay et al., 2017).

**Reticulocytes:** These are immature erythrocytes that have been stripped of their nuclei, and are elevated in some cases of anemia. Normal values are from 0.5 to 1.8% (Buttarello, 2016). An exaggerated elevation of hemolytic crises is usually observed in hemolytic anemia. On the other hand, low levels have been observed in disorders that prevent proper iron utilization, erythropoietin defects and abnormalities in DNA synthesis (Lanzkowsky, 2005; Camaschella, 2017).

**White blood cells:** Also called leukocytes, their main function is to help fight infection. Normal value: 4.5 to 11.0 x 109/L (Etim et al., 2014). Low levels are indicative of marrow deficiency, medications, autoimmune disorders, and diseases caused by microorganisms. A high value is called leukocytosis, which is increased by certain medications, surgery to remove the spleen, infections, and leukemia (Etim et al., 2014; Camaschella, 2017).

**Platelets:** A platelet count may be done to look for the cause of excessive bleeding or clotting. Normal values are 150,000 µL. A low platelet count of 5 is called thrombocytopenia, and this occurs due to insufficient production of platelets in the bone marrow, destruction of the bloodstream, and elimination of the spleen or liver. A large number of platelets is called thrombocytosis due to a type of hemolytic anemia, iron deficiency, bone marrow disease, and splenectomy (Mitrosz et al., 2017; Dobay et al., 2017; Ibrahim, 2018).

**Red Cell Indicators**

Hemoglobin levels are measured by a blood test and are expressed in grams per deciliter (g/dL). A decrease in the level of hemoglobin in the blood is directly related to a decrease in the level of oxygen. Hemoglobin is the first factor to be checked in cases of anemia or iron deficiency problems. Hemoglobin levels at the point where the hemoglobin level is below the reference range, that is, on a complete blood count test, varies according to age and gender (Xiong et al., 2017). If it is below the reference range, the first problem that comes to mind is anemia. Elevated hemoglobin levels may be an indicator of the rare disease polycythemia Vera (Sazawal et al., 2014). High hemoglobin levels can be caused by dehydration, smoking, or living at high altitudes, or it can be related to other conditions such as lung or heart disease (Tham et al., 2018).

Hemoglobin is a substance found in red blood cells that makes it possible for blood to carry oxygen throughout the body (Kosmachevskaya et al., 2021). Hemoglobin is the iron-rich protein that gives red blood cells their colour. Red blood cells carry oxygen throughout the body and need hemoglobin to do so. For red blood cells to move easily through the bloodstream, they must be round and flexible.

The main function of red blood cells is to transport oxygen from the lungs to the cells of the body. Red blood cells actually contain a protein called hemoglobin that carries this oxygen. In the capillaries, oxygen is released for use by the cells of the body. Ninety-seven percent of the oxygen carried by the blood from the lungs is carried through hemoglobin. The remaining 3 percent is dissolved in the plasma. Hemoglobin allows blood to transport 30 to 100 times more oxygen than it can dissolve in plasma alone (Mairbäurl, 2013).

In the lungs where the level of oxygen is high, hemoglobin combines loosely with oxygen (Gupta, 2014). Hemoglobin then releases this oxygen easily into the capillaries where the oxygen level is low (Liu et al., 2018). There are four iron atoms in each hemoglobin molecule. Each iron atom is attached to an oxygen molecule. The iron in hemoglobin is what gives blood its red colour. 33% of red blood cells are hemoglobin (Glenn & Armstrong, 2019).

According to Lippi et al. (2008) Hemoglobin may be requested for a variety of reasons, as part of a complete blood count. It is associated with various diseases depending on whether the result is lower or higher than the reference range. The average concentration of hemoglobin in the body: corresponds to the percentage of hemoglobin in the pressurized red blood cells. Its reference value is 32 to 36 (g/dL), and values below these indicate the amount of hypo pigmented cells in the blood smear (Lee & Powell, 2013).

Average erythrocyte volume: Determines the volume of red blood cells. In addition to identifying standard anemias (85 µl and 100 µl), microcytic (<85 µl) and macrocytic (>100 µl), it will allow us to classify them morphologically, hence the importance of the precision that these parameters must have (Briggs, 2009). Average Muscle Hemoglobin: It is the percentage of hemoglobin that each red blood cell contains on average. Its normal value of 27 to 31 pg. defines the concepts of hypopigmentation, hypopigmentation, and hyperpigmentation (Davidenko et al., 2011).

**Hypothyroidism**

It occurs when there is a change in the thyroid gland that is not sufficiently able to synthesize adequate levels of thyroid hormone as required by the body. Iodine deficiency is currently the leading cause of hypothyroidism worldwide (Zimmermann, 2008). Primary hypothyroidism accounts for 90% of cases with elevated TSH levels and low thyroid hormone in cases where thyroid hormone is elevated. Normal FT4 is called subclinical hypothyroidism (Dubaj et al., 2020).

**Hypothyroidism Associated With Other Systemic Diseases**

The regulation of cellular metabolism occurs thanks to the action of triiodothyronine (T3) and thyroxine (T4), hormones that are also involved in the control of hepatocytes (liver cells), and therefore they modulate the function of the said organ. In the same way, the liver maintains a relationship with the metabolism of hormones produced in the thyroid gland, thus regulating their effect on the body. This association between the two may explain why thyroid changes can disrupt the functions performed by the liver, and in the same way, any liver disease can cause a metabolic disorder of the thyroid gland (Zimmermann, 2008).

These hormones are involved in altering the renin-angiotensin-aldosterone system. Subsequent products obtained from renin are synthesized by the action of triiodothyronine. In poor thyroid condition, diastolic blood pressure often rises, pulse pressure narrows, and renin decreases. This causes sodium-sensitive

hypertension. Erythropoietin secretion increases with T3, which may be related to the anemia found in patients with abnormal thyroid glands (Dubaj et al., 2020).

**Hormonal Therapy**

The drug of choice is levothyroxine because of its high efficacy in treating symptoms of hypothyroidism, it is also well absorbed in the body, causes minimal side effects and has a low cost (Zimmermann, 2008).

**Case Study**

A 55-year-old female patient attends a hospital guard due to dyspnea (dyspnea). The patient reports that she has noticed in recent months a certain shortness of breath due to the efforts made, but this difficulty has intensified in the past hours. There is a doctor on duty, a pale note on both the skin and mucous membranes.

Upon acceptance, the analysis showed the following: Hto 25%; Hb 5 g / dl; GB 3.0 x 109 / L; GR 2.6 x 1012 / L; Platelets 80 x 109 / L; MCH and MCHC normal. VCM 100 hectoliters; Reticulocytes 0.8%; Coombs negative test. In addition, it contains increased LDH and indirect bilirubin. Inform the patient of a varied diet with good meat and vegetable intake. The only antecedents are that he was hypothyroid for 8 years and was treated with thyroid hormone with modern controls with normal levels of the hormone

**Indicative Questionnaire**

Discuss the patient's blood count values, compare with reference values.
Explain the complications that may be associated with reduced values: (a) red blood cells, b) white blood cells, and c) platelets.
What is the likely cause of changes in blood counts?
How do you explain the increase in LDH?

**Methodology**

Descriptive study by reviewing updated scientific articles and clinical hematology guidelines that support the clinical case.

**Case Study Analysis**

In hypothyroidism, anemia is generally normochromic normocytic and of uncertain origin, it is the physiological response to the reduction in erythropoietin production, it may also be due to the deficiency of specific nutrients due to less absorption due to gastric atrophy or hypermenorrhea, causing a great loss of iron that is frequently observed in this type of patient (Elstrott et al., 2020).

The normal anemia in these patients is the most common, the reticulocytes are low or normal, and in these cases pallor, jaundice, coluria, and splenomegaly are observed, the most characteristic form being the form on which it appears. In

association with chronic diseases or inflammatory processes (Davidenko et al., 2011).

According to several authors, anemia of chronic disease, or inflammatory anemia, usually occurs in patients with hypothyroidism, and this can degenerate into hypothyroidism at different stages of the inflammatory process (Lim et al., 2020). Lab tests for people with this condition usually show low blood iron values, transferrin usually normal, but with stable iron stores, and rarely elevated ferritin (Ganz & Nemeth, 2012). Moreover, Thyroid hormone is responsible for stimulating the production of erythropoietin and affects hematopoiesis, an inhibition in the production of thyroid hormone causes anemia ((Zhang et al., 2017; Sánchez et al., 2020).

Despite the fact that these play an important role in erythropoiesis and cell proliferation, there is also an exaggerated consumption of iron, folic acid and cobalamin, which shortens the half-life of the blood components producing leukopenia and plaquetopinia, indicative of bone marrow hypoplasia and associated its hypersplenism in hyperthyroid patients (Carter, 2018). In various biochemical tests, thyroid hormone has been shown to inhibit insulin receptors and increase beta-adrenergic receptors on the surface of leukocytes (Lee, 2020). The percentage of hematological sympathies in patients, cases of anemia can be observed usually 10-34%, leukopenia, neutropenia generally 15-30%, thrombocytopenia 2-5%, pancytopenia 23% (Carter, 2018).

The diagnosis of anemia of chronic disease is associated with the exclusion of other types of anemia, including iron deficiency anemia. Although both types of disorders have a common deficiency in this component, there are several related characteristics that allow them to be distinguished (Ganz & Nemeth, 2012). When assessing the causes of anemia in chronic diseases, it is worth highlighting the change in the production of hemoglobin, the deficient hemolytic component of this disease, as well as the complex humoral and cellular regulation of the hematopoietic process (Ganz & Nemeth, 2012).

Inflammatory anemia has a variety of causes. It presents a complex process characterized by reduced erythropoiesis, inhibition of immature erythrocytes in the bone marrow, and increased levels of inflammatory cytokines (IL-1, IL-6, IFN-α1, IFN-β1, and TNF-α), closely associated with decreased different stages of erythrocyte development. Red blood cells, which eventually leads to iron-limiting erythropoiesis (Lee, 2020). In addition, Erythropoietin deficiency or hyposensitivity to target tissues is one of the mechanisms for the development of anemia of chronic disease (Lim et al., 2020).

Cytokines and retinal endothelial cells are stimulated and, as a result, they will cause changes in the internal iron balance, there will be a decrease in the response in erythrocytes, the half-life of red blood cells is shortened, and proliferation and differentiation will also show a decrease in blood cell precursors (Bocci et al., 2009). These cytokines stimulate an increase in Hepcidin, a hormone produced in the liver that plays a key role in iron homeostasis, is of high value in inflammatory anemias, and acts detrimentally by blocking iron transport (Ganz & Nemeth, 2012).

According to the clinical picture, the patient shows pancytopenia, and highlights in the analyzes, severe anemia with the characteristics of being normal, normal in color, presenting normal erythrocyte values, with a reticulum value of 0.8% (normal value 0.5 to 1.5%); Any presence of regenerating bone marrow (Gholipourmalekabadi et al., 2015), a negative Coombs test ruling out a type of autoimmune anemia, as well as an increase in lactate dehydrogenase (normal value 0.6 to 1.0 mg/dL), elevated indirect bilirubin (normal value 0.2 at 0.7 mg/dL). deciliter), with a value significantly higher than normal, indicates an increase in the destruction of red blood cells. In addition, the patient shows a normal average-sized erythrocyte volume (28 to 32 pg%), so she has hemochromatosis normal (Sanju, 2019).

In anemia of chronic disease, the body cannot use the iron that is naturally obtained and absorbed for use by red blood cells to synthesize hemoglobin, instead it is stored in myeloid macrophages and is not released. Therefore, red blood cells have a shorter-than-normal half-life of 120 days and poor response to erythropoietin (Lee, 2020). The regenerative marrow can also produce this anemia. Due to iron deficiency for erythropoiesis, normal values of hematocrit and hemoglobin decrease before the volume of red cells, which is manifested in normal anemia (Buttarello, 2016).

To determine the diagnosis, two primary criteria must be presented: serological evidence of autoantibodies and laboratory evidence of hemolysis. The direct Coombs test is responsible for detecting autoantibodies on the surface of red blood cells (Zhang et al., 2020; Salama et al., 2004). It is performed by adding monoclonal anti-IgG, anti-IgM and anti-C3d serum to wash out the patient's red blood cells. If obliterated, agglutination is observed, which is considered a positive Coombs test (Zhang et al., 2020).

Destroying too many red cells will result in the production of a high level of bilirubin and lactate dehydrogenase in the blood (Asleh et al., 2019). In the case of a hemolytic syndrome patient, it is necessary to determine the time of development of anemia, which will help us clarify whether it is a recent condition or is it associated with a chronic process. The most appropriate test is the direct Coombs test; this allows determining that the anemia is caused by serum antibodies or complement activity. When a negative result in this test is obtained, a type of hemolysis caused by the immune response is excluded (Zhang et al., 2020).

In biochemical tests of these patients, there is an increase in lactate dehydrogenase due to red blood cell rupture, an increase in total bilirubin in direct proportion to indirect bilirubin (hemoglobin synthesis by hemolysis), and a decrease in serum heptoglobin and hemoglobin (proteins) that capture increased amounts in the free circulating hemoglobin) (Asleh et al., 2019).

**Conclusion**

Anemia is a common condition in patients with thyroid disorders. By investigating scientific articles, it was possible to establish that changes in the concentration of hemoglobin, hematocrit, indices of erythrocytes and the number of red blood cells

affect the development of this pathology. The reduced production of erythropoietin, the reduced half-life of red blood cells and the proliferation of blood cell precursors in the bone marrow made it possible to establish an association between patient symptoms and prevailing laboratory findings between anemia and hypothyroidism.

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