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# IRON DEFICIENCY AND IMPORTANCE OF NUTRITIONAL INTERVENTION IN IRON DEFICIENCY ANEMIA
# DEMİR EKSİKLİĞİ VE DEMİR EKSİKLİĞİ ANEMİSİNDE BESLENME MÜDAHALELERİNİN ÖNEMİ

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## ABSTRACT

**Introduction:** Iron deficiency is the most prevalent micronutrient deficiency globally. It leads to high rates of anemia in children, particularly in developing countries, and is common among women of reproductive age. Iron deficiency is a global public health issue with implications for both individual health and broader social and economic impacts. It leads to various health problems, ranging from increased risk of preterm birth and cognitive and physical developmental issues in children to reduced work productivity and physical performance in adults. Iron is found in two forms in foods and plays a vital role in essential biochemical processes such as oxygen transport, tissue oxygenation, and DNA and protein synthesis. The deficiency arises from an imbalance between iron intake and absorption and the body's needs. Iron absorption mostly depends on factors such as the existing amount of iron in the body and the quantity, form, and bioavailability of iron in the diet.
**Aim:** The aim of this study is to highlight the importance of iron deficiency and nutritional aspect of iron deficiency anemia.
**Methods:** Original articles and literature reviews in PubMed, Web of Science, Elsevier Science Direct, and Springerlink databases were conducted using keywords such as iron deficiency anemia, anemia, and nutrition intervention in iron deficiency anemia.
**Conclusion:** Adjusted dietary habits, iron supplementation, and awareness are critical factors in preventing and treating iron deficiency anemia.

**Keywords:** Anemia, Iron, Iron Deficiency, Iron Deficiency Anemia, Nutritional Intervention in Iron Deficiency

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**ÖZET**

**Giriş:** Demir eksikliği, dünya genelinde en yaygın görülen mikro besin eksikliğidir. Gelişmekte olan ülkelerde çocuklarda yüksek oranda anemiye yol açar ve bu eksiklik, özellikle üreme çağındaki kadınlarda yaygındır ve hem birey sağlığı hem de sosyal ve ekonomik yansımaları olan küresel bir halk sağlığı sorunudur. Bu durum, erken doğum riskinden çocuklarda bilişsel ve fiziksel gelişim bozukluklarına, yetişkinlerde ise iş verimliliği ve fiziksel performans düşüklüğüne kadar çeşitli sağlık sorunlarına neden olur. Demir, besinlerde iki formda bulunur ve oksijen taşıma, doku oksijenasyonu, DNA ve protein sentezi gibi hayati biyokimyasal süreçlerde rol oynar. Eksikliği, demir alımı ve emilimi ile vücudun ihtiyaçları arasındaki dengenin bozulmasından kaynaklanır.
**Yöntem:** Bu derleme, PubMed, Web of Science, Elsevier Science Direct and Springerlink veri tabanlarından demir eksikliği, demir eksikliği anemisi, demir eksikliği anemisinde beslenme anahtar kelimeleri kullanılarak araştırma ve derleme makaleleri taranarak oluşturulmuştur.
**Amaç:** Bu çalışmanın amacı demir eksikliğinin ve demir eksikliği anemisinin önemini vurgulayıp beslenme stratejilerini ele almaktır.
**Sonuç:** Beslenme düzenlemeleri ve demir takviyeleri, demir eksikliği anemisinin önlenmesi ve tedavisinde kritiktir. Demir emilimi, vücutta mevcut demir miktarı, beslenmedeki demirin miktarı, biçimi ve biyoyararlılığı gibi faktörlere bağlıdır.

**Anahtar Kelimeler:** Anemi, Demir, Demir Eksikliği, Demir Eksikliği Anemisi, Demir Eksikliği Anemisinde Beslenme

## 1. INTRODUCTION

It is a mineral that constitutes the mostly of hemoglobin. It is a vital mineral that plays a crucial role in oxygen transportation within the human body. It acts as a catalyst for certain enzymes that are involved in energy production, cell growth and proliferation, neurotransmitter and protein synthesis, oxygenation of muscles, and gene regulation (Piskin et al., 2022). The typical adult human body contains between 4 and 5 grams of iron. While approximately 60-70% of the iron is present in hemoglobin and erythrocytes for the transportation of oxygen, 10% is found in myoglobin, cytochromes, and iron-containing enzymes. The remaining 20-30% is stored in the liver and macrophages of the reticuloendothelial system in case of need (Bulut, 2017). The storage form of iron in the human body is known as ferritin or hemosiderin. The liver and bone marrow account for approximately one-third of the ferritin stores. Each gram of ferritin contains 8 ng of stored iron and is subject to age- and gender-related variations. Serum ferritin levels may increase in the presence of infectious diseases, liver and kidney diseases, and malignant diseases.

## 2. DIET SOURCES OF IRON

Iron is present in dietary sources in two forms such as heme and non-heme. The heme form is exclusively present in foods of animal origin, namely meat, fish, and poultry. This form of iron is the most readily absorbed by the body from the stomach. The non-heme form is also present in plant foods, in the same manner as it is found in meat (Table 3). The iron present in these foods is not absorbed as completely as that which is present in heme. The absorption rate is 25-30% for heme iron and 4% for non-heme iron (Piskin et al., 2022). There are multiple methods that can be employed to enhance iron absorption (Table 1).

**Table 1.** Factors Affecting Iron Absorption

| Factors Increasing Iron Absorption | Factors Decreasing Iron Absorption |
|---|---|
| *Vitamin C* helps the body absorb non-heme iron and is found in citrus fruits, tomatoes, broccoli, and strawberries | The consumption of coffee, even in its decaffeinated form, reduces the absorption of iron |

| | |
|---|---|
| Eating heme-rich foods together with non-heme-rich foods | Tea, even in its decaffeinated form, has been shown to reduce the absorption of iron |
| Cooking non-ferrous foods in iron cookware, such as cast-iron pans | Excessive consumption of high-fiber foods |
| | Calcium intake two hours after consuming meals high in iron |

The Recommended Daily Allowance (RDA) for iron is 8 mg per day for adult men aged 19-50 years, 18 mg for women, 27 mg for pregnant women, and 9 mg for lactating women (Table 2) (Institute of Medicine, 2001). The elevated levels in women and during pregnancy are attributable to blood loss through menstruation and the accelerated growth of the fetus, which necessitates enhanced blood circulation during pregnancy (Institute of Medicine, 2001).

**Table 2.** Recommended Daily Allowance of Iron for Non-Vegetarians

| **Age** | **Female** | **Male** | **Pregnancy** | **Lactation** |
|---|---|---|---|---|
| Birth to 6 months | 0.27 mg | 0.27 mg | | |
| 7-12 months | 11 mg | 11 mg | | |
| 1-3 years | 7 mg | 7 mg | | |
| 4-8 years | 10 mg | 10 mg | | |
| 9-13 years | 8 mg | 8 mg | | |
| 14-18 years | 15 mg | 11 mg | 27 mg | 10 mg |
| 19-50 years | 18 mg | 8 mg | 27 mg | 9 mg |
| 51+ years | 8 mg | 8 mg | | |

Source: Institute of Medicine, 2001

**Table 3.** Contents of the Average Amount of Iron in 100 g

| **Food** | **Iron Amount (mg)** | **Food** | **Iron Amount (mg)** |
|---|---|---|---|
| Veal liver | 4,50 | Hazelnut | 3,10 |
| Beef | 1,81 | Almond | 5,26 |
| Chicken | 0,31 | Walnut | 2,34 |
| Fish | 0,72 | Peanut | 2,30 |
| Egg | 1,83 | Bread (whole wheat) | 1,76 |
| Lentil | 5,87 | Bread (white flour) | 1,00 |
| Chickpeas | 5,92 | Spinach | 9,71 |
| Bean | 4,71 | Cress | 11,74 |
| Grape molasses | 1,60 | Arugula | 6,11 |
| Tahini | 6,01 | Parsley | 4,76 |
| Raisins | 5,08 | Lettuce | 2,51 |

Source: National Food Composition Database. Turkey, 2019

## 3. ANEMIA AND IRON DEFICIENCY ANEMIA

Hemoglobin (Hb), hematocrit (Htc), and erythrocyte count (RBC) reductions that are two standard deviations below the age and gender-specific mean are referred to as anemia. Different forms of anemia can arise from a variety of reasons (Table 4). Iron deficiency (ID) is characterized by a decrease in the body's iron reserves along with a restriction in hemoglobin production because there is insufficient iron available to support erythropoiesis. When hemoglobin levels fall below -2SD and the disease persists, it is characterized as iron deficiency anemia (IDA) (World Health Organization, 2001). IDA represents a significant global public health concern, affecting both developed and underdeveloped countries. It has been linked to adverse outcomes on individual health and quality of life, as well as social and economic repercussions. The condition is particularly prevalent among women of reproductive age. The primary determinants of IDA are heavy menstrual bleeding, pregnancy status, and the postpartum period (Critchley, 2020; Cappellini, 2022). Each of these factors carries its own independent risks and should therefore be considered individually.

**Table 4.** Types of Anemia

| **Anemia Type** | **Cause of Anemia** |
|---|---|
| Aplastic Anemia | The stem cells in the bone marrow are damaged and are not able to produce enough blood cells. |
| Hemolytic Anemia | When red blood cells (RBCs) are destroyed and removed from the bloodstream before completing their normal lifespan. |
| Autoimmune hemolytic anemia | A type of anemia characterized by antibodies produced by the immune system attacking red blood cells and shortening the lifespan of erythrocytes. It is the main cause of hemolytic anemia. |
| Iron Deficiency Anemia | A form of anemia that results from insufficient iron intake, impaired iron absorption, or blood loss. |
| Sickle Cell Anemia | A genetic disorder in which the structure of hemoglobin assumes a "c-shape," thereby impairing its ability to fulfill its function and resulting in a reduction in the number of red blood cells in the blood. |
| Thalassemia | Defined as a blood disorder that affects the production of red blood cells. |

| | |
|---|---|
| Pernicious Anemia | A condition characterized by insufficient vitamin B12 levels, which impairs the body's ability to produce sufficient healthy red blood cells. |
| Pyruvate Kinase Deficiency | A type of anemia that develops due to a deficiency of pyruvate kinase in red blood cells. The deficiency of pyruvate kinase results in the breakdown of red blood cells. |
| Hereditary Elliptocytosis | Congenital disorders of the red blood cell membrane are caused by a deficiency of the enzyme glucose-6-phosphate dehydrogenase in red blood cells. |

## 4. PREVALENCE OF IDA

IDA is the most common anemia condition, affecting all population groups worldwide and causing approximately 840,000 deaths (World Health Organization, 2022). It ranks ninth among 26 modifiable mortality risk factors in the Global Burden of Disease project (Collaborators, 2016). From the prevalence analysis of Hb or Hct levels outside the ideal range determined by WHO, anemia was classified in terms of public health and it was stated that if it is 5% and above, it is a mild public health problem, moderate at 20-39.9%, and serious at 40% and above (Sanrı, 2014). According to WHO, 40-89% of anemia in women is characterized as iron deficiency anemia. This rate is 22.9% in Europe and 27.8% in Türkiye (World Health Organization, 2015; Saydam, 2017). It has also been reported that 36.5% of all pregnant women in the world are anemic (Wenzel, 1962). South Asia is a region where anemia is especially common. In Africa, anemia affects 40% of non-pregnant women and 50% of pregnant women. Pregnant and non-pregnant women in Latin America and the Caribbean had anemia prevalence rates of about 40% and 30%, respectively (Stevens et al., 2022). According to 2019 data, the prevalence of anemia in women of reproductive age was reported as 38.8% in low-income countries and 14.4% in high-income countries (Baysal et al., 2016). While two-thirds of women in Türkiye experience iron deficiency anemia (ID) during their reproductive age, one-third of women in the same period experience iron deficiency anemia (IDA) (Özkan, 2018). In 2011, the prevalence of anemia in Türkiye was 28.86% (Özkan, 2018). In 2016, this rate was reported as 30.87% (World Health Organization, 2021). In developing countries, the prevalence of anemia in young children is approximately 50%, with approximately half of this anemia thought to be caused by ID (Mantadakis, 2020). Additionally, dietary modifications may serve as an adjunct to pharmacological intervention, offering supplementary nutrients and preventing unfavorable interactions between nutritional supplements and food. Furthermore, the long-term strategies of food fortification and iron supplements can be employed to reduce and control the prevalence of IDA.

## 5. POPULATION AT RISK

During pregnancy, women's iron requirements increase to meet the needs of the developing fetus and the placenta (World Health Organization, 2001). This need is particularly high for preterm or low birth weight infants and infants whose mothers are iron deficient (Black, 2011; Domellöf, 2011). The risk of

menorrhagia in women of reproductive age and iron deficiency is increased in frequent blood donors (Institute of Medicine, Food and Nutrition Board, 2001). A review of the literature reveals that approximately 25-35% of regular blood donors experience iron deficiency (Kiss, 2015). Additionally, studies indicate that frequent donors are five times more likely to deplete iron stores than first-time donors (Kiss, 2015; Cable, 2011). Similarly, cancer patients are at an elevated risk of iron deficiency. A meta-analysis of 11 studies revealed that 60% of colon cancer patients and 29-46% of patients with other types of cancer exhibited iron deficiency (Aapro, 2012). Moreover, individuals with gastrointestinal disorders, such as celiac disease, ulcerative colitis, and Crohn's disease, or those who have undergone specific surgical procedures, are prone to developing iron deficiency due to dietary restrictions (Bayraktar, 2010; Bermejo, 2009).

## 6. ASSESSMENT OF IDA

A number of parameters are employed in order to detect iron deficiency anemia (Table 5). The initial parameter is serum iron concentration. The serum iron concentration level may be observed as low or within the normal range on the IDA. The highest levels are observed in the morning, with a subsequent decline throughout the day. The levels of the biomarker in question are observed to decrease in instances of inflammation and malignancy, as well as during the menstrual cycle. Serum iron concentrations are not employed as a diagnostic tool, given that they are susceptible to influence by a range of conditions. Another parameter, total iron-binding capacity (TIBC), represents the supply of iron to tissues. In the context of chronic disease, TIBC is typically reduced, whereas in cases of iron deficiency, it is elevated. Transferrin Saturation is defined as the ratio of serum iron to total iron-binding capacity (TIBC). In cases of iron deficiency, saturation levels are observed to decline. Conversely, in instances of chronic disease, saturation levels are typically found to be within the normal range. Serum ferritin levels serve as a reflection of the total body iron stores. A serum ferritin level of 10 ng/ml is considered diagnostic for (IDA). Elevated levels are observed in conditions characterized by inflammation, infection and liver disease. The impact of infections on serum ferritin frequently constrains its capacity to serve as a precise indicator of iron stores, particularly in regions where the prevalence of infection is markedly elevated (Table 6.).

**Table 5.** Parameters Used For Iron-Deficiency Anemia

| Parameters | Iron Deficiency Anemia | Iron Stores |
|---|---|---|
| Transferrin | Low level | Normal level |
| Hemoglobin | Low level | Normal level |
| Plasma Ferritin | Low level | Low level |
| Erythrocyte Protoporphyrin | High level | Low level |

**Table 6.** Stages of Iron Deficiency

| Stage 1 | Stage 2 | Stage 3 |
|---|---|---|
| • Decrease in iron stores<br>• Not linked to detrimental physiological effects | • Decreased tranferrin saturation<br>• Increased erythrocyte protoporphyrin, and increased serum transferrin receptor levels. | • Hemoglobin levels are below 7g/dl.<br>• Iron deficiency anemia begins to appear |

## 7. NUTRITION IN IRON DEFICIENCY ANEMIA

It is a well-established fact that iron supplements represent the most common method of preventing iron deficiency. However, in addition to this approach, the World Health Organization (2008) identifies two further potential avenues for treatment: firstly, the elimination of the underlying factors that cause iron deficiency and secondly, the elimination of other nutritional deficiencies. The most effective method for preventing iron deficiency is exclusive breastfeeding, particularly during the first six months of life. This is because the majority of iron in breast milk is absorbed (Iron Utilization Survey Report in 12-23 Month-old Children, 2009). However, after six months, breast milk alone may be insufficient to meet the increasing iron requirements of the infant. Therefore, foods containing additional iron sources should be included in the diet. The absorption of iron is contingent upon a number of factors, including the quantity of iron present within the body, the amount, form, and bioavailability of iron in the diet (Yurdakök K, 2009). When it comes to iron content and ease of absorption, meats are the greatest source; other excellent sources of iron include eggs, molasses, dried fruits, oilseeds, legumes, and green vegetables (Baysal, 2009). Eggs, cereals, vegetables, and fruits do not absorb ferric iron as well as meat, fish, and poultry do (Zhu, 2017). Moreover, diets heavy in carbs and low in meat have been shown to decrease blood iron levels (Bansal K, 2016). Well-fermented bread is favored because it breaks down the acids in flour that inhibit iron use, even though yeast is rich in iron (Baysal, Bozkurt, Güneyli, & Aksoy, 1983; Neyzi, 1984). Breads without leavening may reduce the absorption of iron (Yurdakök K, 2009). Iron absorption is also influenced by cooking times and temperatures; long cooking times and high temperatures might have a detrimental effect on absorption (Yurdakök K, 2009).

## 8. CONCLUSION

Iron is a vital micronutrient for the human body, serving multiple functions, and its deficiency may lead to various pathologies, including iron deficiency anemia when there is an imbalance between iron needs and intake. The effective method for treating anemia through nutritional approaches involves multiple strategies. While increasing iron intake , particularly heme iron, absorption inhibitors should not be present in the meal at the same time. Consideration should be given to the use of bioavailability enhancers for non-heme sources of iron. Preventive treatment approaches should focus on maintaining balanced and adequate nutrition from birth to prevent iron deficiency anemia. In conclusion, addressing iron deficiency anemia effectively requires considering the complexity of nutritional approaches and various influencing factors.

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