Impacts of Acquired Iron Deficiency on Adolescent Health

Luiz Antonio Del Ciampo1* and Ieda Regina Lopes Del Ciampo2

1Department of Puericulture and Pediatrics, Faculty of Medicine of Ribeirão Preto, University of São Paulo, Brazil.
2Department of Medicine, Federal University of São Carlos, São Paulo, Brazil.

Authors’ contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

ABSTRACT

Adolescence is a period of growth and physical and emotional development for which, among other factors, it is necessary to ingest nutrients in sufficient quantity and quality to supply all the demands of the organism. As it is a phase of nutritional vulnerability, adolescents need to have their nutritional status monitored to prevent the lack of micronutrients from interfering with their full growth and development. Iron is a fundamental micronutrient for humans and its lack can lead to several physical and emotional impairments that interfere with good health conditions. This article presents the characteristics of the adolescent's growth and development and the consequences that can be caused by acquired iron deficiency during the second decade of life, with repercussions that can extend throughout adult life. It also proposes measures to prevent or minimize this nutritional problem among adolescents.

Keywords: Adolescence; adolescent development; iron deficiency; anemia.

*Corresponding author: Email: delciamp@fmrp.usp.br;
1. INTRODUCTION

Iron is an essential micronutrient for all tissues of the developing body and iron deficiency (ID) from mild forms to more severe cases of anemia, is the most prevalent nutritional deficiency worldwide, affecting mainly populations from less developed countries, of all age groups, including adolescents [1]. Recent studies show that the prevalence of (ID) among adolescents has varied between 8.06% in Kuwait [2], 10.9% in Nepal [3], 13.3% in Spain [4], 21.3% in India [5] and 23% in Indonesia [6], which confirms the current worldwide extent of this public health problem. Currently, there are more than 1.2 billion adolescents worldwide who, due to their physical and emotional characteristics, constitute an age group of high vulnerability in relation to iron deficiency and its consequences [7].

2. ADOLESCENT’S VULNERABILITY TO ACQUIRED ID

Some characteristics of adolescents make them more susceptible to acquired iron deficiency and must be known to provide the best conditions for growth and development.

a) Growth

Adolescence is a phase of great physical, emotional, and social changes that the individual goes through, evolving from childhood to adulthood. For this, the human being suffers multiple influences from the environment, which acting on his genetic potential will trigger the processes of accelerating growth, modification of body composition and sexual maturation, that occurs between 10 and 20 years of age [8]. These process of growth and development is a complex, continuous, and non-uniform event, which promotes the necessary physiological changes to transform the individual into an adult being [9].

Among the stages of growth with increased speed, adolescence stands out as the second fastest period, when the pubertal spurt occurs, which is responsible for increasing weight, height and changes in body composition, adding to bone tissue, fat and muscle mass [10]. The increase in the adolescent’s body dimensions is related to the growth that reaches its peak velocity during puberty. Girls can grow up to 9 cm/year, reaching between 15% to 25% of adult height during this period, while 50% of adult weight is gained in adolescence. In turn, boys can grow between 10 and 12 cm/year and acquire almost half the adult’s weight during the pubertal spurt [11,12].

This great speed of weight and height gain is reflected in the incorporation of tissues and organs that need to be irrigated, which demands an increase in the volume of circulating blood, estimated at 75 mL/kg of weight. This expansion of blood volume, with a consequent increase in the number of red blood cells, requires greater amounts of iron by the body. In addition, iron is being used for the synthesis of enzymes, heme proteins, myoglobin and incorporated in several types of cells [13,14]. In female adolescents, menstrual blood loss (on average 0.47 mg / day) makes them particularly vulnerable to iron deficiency compared to men [15]. And in some cases, these losses of iron can be exacerbated when the adolescent presents heavy menstrual bleeding that occurs due to the immaturity of the hypothalamic-pituitary-ovarian axis [16].

b) Eating habits

A proper diet should provide enough iron and nutrients that support bioavailability for needs at this stage of life. A common characteristic among adolescents refers to the change in eating habits due to the influence of peers, the need for family self-affirmation or due to the behavioral or social changes that they face in this phase. In adolescence, eating disorders can include refusal to eat, skipping breakfast, replace the main meals for snacks, reducing intake of fruits and vegetables, and adopt diets for excessive weight loss, all because of the undue importance given to body image as a result of inadequate publicity in the media and the cult of ultrafine models, often malnourished [17,18]. Another important aspect refers to the consequences of the increasing dependence on fast food, due to its availability and ease, which is potentially harmful due to nutritional characteristics that include high energy, fat and sodium and low fiber, vitamins, calcium and iron content [17-19]. In addition, the consumption of restrictive diets, mainly vegetarian and vegan, is increasing among adolescents, mainly in the western world, becoming potentially critical for adolescents with risks of inadequate supply of various nutrients, including iron [20-22]. Vegetarian diets when not accompanied by adequate supplemental iron intake can contribute to the installation and maintenance of the deficiency state of this mineral [23,24]. Other important aspect to be considered is that adolescents have increased the consumption of energy drinks with high levels of caffeinated energy drinks and carbonated...
beverages which, among other effects on metabolism, can interfere with iron absorption [25, 26].

3. IRON AND ITS IMPORTANCE FOR THE HUMAN ORGANISM

Iron performs multiple vital functions in many biochemical reactions in the human body including carrying of oxygen from lung to tissues, transport of electrons within cells, acting as co-factor for essential enzymatic reactions, and synthesis of steroid hormones. Most of the iron in the human body is found in the ferrous state, in a complex form with a protoporphyrin (heme) ring, mainly in the protein hemoglobin and myoglobin [27]. The remainder of iron is in the form of polynuclear complexes of ferric oxy-hydroxide-phosphate, such as ferritin, hemosiderin, non-heme enzymes, mitochondrial cytochromes, catalase, and transferrin [28].

In the diet, iron is present in red meat, eggs, vegetables, and grains. Iron absorption is influenced by physiological factors that affect its availability and is controlled by the amount taken up by the intestinal mucosa in response to the body’s needs. The chemical form of iron is an important factor that affects its availability in different types of diets [29]. Heme iron that is present in animal foods, such as meats, chickens and fish is easily absorbed by the intestinal mucosa, and this absorption is facilitated by the presence of vitamin C. Inorganic forms of iron, association with fructooligosaccharides and ferrous salts are more readily absorbed than ferric salts. The greatest absorption occurs in the upper duodenum due to the acidic environment. [17]. The bioavailability of iron in the diet can be reduced by the phytic acid found in whole grains, vegetables, lentils, and nuts; polyphenols, such as tannic and chlorogenic acids, found in tea, coffee, red wines and a variety of cereals, vegetables and spices; soy protein and eggs [30].

Iron needs are determined by the demand for tissue development, increased erythrocyte mass and hemoglobin concentration and replacement of physiological losses through urine, feces, sweat and menstruation.

4. IRON DEFICIENCY

Iron deficiency occurs due to a negative iron balance caused by inadequate intake (low amount and / or bioavailability), increased needs and chronic blood loss (occult gastrointestinal bleeding in parasitic diseases, shedding of skin, and epithelial cells). This condition is responsible for low supply oxygen to tissues compromising cell proliferation and differentiation, growth, myelogenesis, immune function and energy metabolism [32]. Iron deficiency anemia is the most advanced stage of iron deficiency, which is characterized by depletion of iron stores, low levels of hemoglobin and hematocrit and decreased transferrin saturation [33].

Table 1. Daily iron requirements (mg/day)* for adolescents

| Age (years) | Female | Male |
|-------------|--------|------|
| 10 - 13     | 8      | 8    |
| 14 - 18     | 11     | 15   |
| ≥ 19        | 8      | 18   |

* Modified from IOM [31]

Signs and symptoms of ID are generally vague, nonspecific and can be associated with some clinical conditions. In most cases, the onset of iron deficiency is insidious and there are no clinical manifestations, which will appear gradually as the amount of iron in the body decreases. Table 1 shows the main clinical changes related to low iron concentrations in the body. Fatigue, indisposition, changes in mood and appetite, headaches, cheilosis, atrophic glossitis, dry mouth, hair loss, dry skin, and nail deformities are some of the common manifestations, which increases the importance of clinical history and the support of laboratory tests [33, 34]. These consequences result from insufficient iron-dependent functioning for oxygen transport and cellular/tissue metabolism.

Table 2. Clinical changes due to ID

| Clinical manifestation          | References |
|--------------------------------|------------|
| Fatigue                        | 1,31,32,33 |
| Indisposition                  | 1,31,32,34 |
| Changes in mood                | 1,33,34    |
| Altered appetite               | 1,32,33,34 |
| Cheilosis                      | 31,32      |
| Dry mouth, atrophic glossitis  | 31,35      |
| Hair loss                      | 32,35,36   |
| Dry skin and nail deformities  | 34,35,37   |

The diagnosis of ID is based on a complete medical history, a detailed physical examination and laboratory tests. Low serum ferritin levels are the hallmark of absolute iron deficiency,
reflecting depleted stocks that identify mild cases [17,38,39].

Although serum ferritin levels may vary according to sex, age group and associated conditions such as the presence of infection, values below 30 ng/mL have been considered sufficient for the diagnosis of ID [40]. Other laboratory tests can also be used, such as: serum iron dosage, total iron binding capacity, transferrin saturation, serum transferrin receptor level and reticulocyte hemoglobin concentration [34].

5. CONSEQUENCES OF ID ON THE CENTRAL NERVOUS SYSTEM OF ADOLESCENTS

The adolescent's neurological development occurs heterogeneously, in the caudal-rustic sense, with different speeds and directed towards the acquisition of executive skills, the search for immediate rewards and emotional regulation to overcome the transformational events that occur during this period of life [41,42]. Structural and functional maturation of the central nervous system in adolescence is characterized by a decrease in the volume of cortical gray matter, a progressive increase in the volume and density of white matter, overproduction of axons, pruning, myelination, refinement of synaptic connectivity and growth of dendrites [43].

Iron deficiency results in several effects on neural function because iron proteins play important roles in normal brain development, neurogenesis, myelination, synaptogenesis, neurotransmission, and metabolism [44,45]. Among the different structures that can be affected, the prefrontal cortex stands out, which plays an important role in decision making, regulation of emotions, attention, perception, memory, and cognition [46].

It has been shown that ID causes negative effects on adolescent development, especially on cognitive and academic performance, learning ability, attention span, perception functions, intelligence, and motor skill [44]. ID leads to a decrease in cognitive scores demonstrated by poor school performance in mathematics and low scores in verbal learning, attention, intelligence assessments, behavioral problems, and mental balance [47-49]. ID has also been linked to emotional changes such as feelings of fear, anxiety and different degrees of depression, which become particularly important during the adolescent's personality development process [50,51].

Therefore, even with nonspecific and apparently mild symptoms (such as irritability, changes in mood, pattern and sleep and emotions) [52]; sleep disorders [53], sometimes confused with normal aspects of adolescence, ID has been associated with slower performance on tasks that measure abstraction and mental flexibility and spatial processing capacity [54]. All alterations, occurring during the second decade of life, can compromise the maturity and future quality of life of this adolescent.

6. ID PREVENTION

Prevention of ID requires social and health actions because the symptoms are vague and can easily be missed. From a medical point of view, it is essential that in all adolescent care a complete clinical history, including eating habits, is obtained. In addition, it is also necessary to identify factors that can compromise the use of iron such as the consumption of foods that contain iron absorption inhibitors (phytic acid in legumes and grains, carbonated drinks, coffee, tea, chocolate and fibers) close to or together with large meals or increase its losses, such as infectious and parasitic diseases [55].

As for food, it is essential to promote the consumption of a varied and balanced diet, containing foods rich in iron, fruits and vegetables rich in vitamin C, which can facilitate absorption and promote benefits in the present and in your future health [56]. In some situations, and according to social and economic conditions, it is also possible to propose the use of iron supplementation during the most critical periods of growth and development [57]. Iron supplementation aims to replenish body stores and prevent chronic deficiency from causing further damage to individuals. It is indicated for iron deficiency states secondary to conditions that can be reversible, especially in situations with increased needs for body iron and low dietary intake [58].

7. CONCLUSIONS

Iron deficiency, although it is a preventable and easily treatable condition, can be responsible for important physiological repercussions with decrements in energy, activity, quality of life, and
work productivity. Furthermore, and especially severe during adolescence, causes cognitive impairment in an important phase of evolution of maturity, which may compromise the quality of life in the future [39]. Therefore, it is necessary that efforts be made in the public health area to identify the causes of iron deficiency among adolescents and to implement measures that aim to eradicate or minimize its effects on adolescents.

**COMPETING INTERESTS**

Authors have declared that no competing interests exist.

**REFERENCES**

1. WHO. Nutritional anaemias: tools for effective prevention and control. ISBN 978-92-4-151306-7 – Geneva. 2017:96.
2. Shaban L, Al-Ta'ar A, Rahman a, Al-Sabah R, Mojmimiyi O. Anemia and its associated factors among Adolescents in Kuwait. Sci Rep. 2020;10:5857.
3. Ford ND, Bicha R, Parajuli KR, Paudyal N, Joshi N, Ralph D. Whitehead Jr RD. Factors associated with anaemia among adolescent boys and girls 10–19 years old in Nepal. Matern Child Nutr. 2020:e13013.
4. Ibáñez-Alcalde MM, Vázquez-López MA, López-Ruiz S, Lendinez-Molinos FJ, Bonillo-Perales A, Parrón-Carreño T. Prevalence of iron deficiency and related factors in Spanish adolescents. Eur J Pediatr. 2020. [Online ahead of print].
5. Samal A, Porwal A, Ramesh S, Agrawal PK, Acharya R, Johnston R. Characterization of the types of anaemia prevalent among children and adolescents aged 1-19 years in India: a population-based study. Lancet Child Adolesc Health. 2020;4:515-525.
6. Andriastuti M, Ilmana G, Nawangwulan SA, Kosasih KA. Prevalence of anaemia and iron profile among children and adolescent with low socio-economic status. Int J Ped Adol Med 2020;7(2020):68e92.
7. United Nations. World Population Prospects; 2019. Available:https://population.un.org/wpp/ Accessed in August 20,2020.
8. Soliman A, De Santis V, Elalaily R. Nutrition and pubertal development. Indian J Endocr Metab 2014;18:39-47.
9. Sawyer SM, Azzopardi PS, Wickremarathne D, Patton GC. The age of adolescence. Lancet Child Adolesc Health. 2018;2:223-228.
10. Greydanus DE, Patel DR, Pratt HD. Essential adolescent medicine. McGraw Hill, New York; 2005.
11. World Health Organization. Issues in Adolescent Health and Development: Nutrition in Adolescence – Issues and Challenges for the Health Sector. Geneva: Switzerland: World Health Organization; 2005.
12. Christian P, Smith ER. Adolescent undernutrition: global burden, physiology, and nutritional risks. Ann Nutr Metab 2018;72:316–328.
13. Tesfaye M, Yemane T, Adisu W, Asres Y, Gedefaw L. Anemia and iron deficiency among school adolescents: burden, severity, and determinant factors in southwest Ethiopia. Adolesc Health Med Ther. 2015;6:189-196.
14. Powers JM, Buchana GR. Disorders of iron metabolism: new diagnostic and treatment approaches to iron deficiency. Hematol Oncol Clin North Am. 2019;33:393-408.
15. Wan D, Wu Q, Ni H, Liu G, Ruan Z, Yin Y. Treatments for iron deficiency (ID): prospective organic iron fortification. Curr Pharm Des. 2019;25:325-332.
16. O’Brien S. Evaluation and management of heavy menstrual bleeding in adolescents: the role of the hematologist. Hematol Am Soc Hematol Educ Program. 2018;1:390-398.
17. Cairo RCA, Silva LR, Bustani NC, CMarques CDF. Iron deficiency anemia in adolescents; a literature review. Nutr Hosp. 2014;29:1240-1249.
18. Alfaris NA, Al-Tamimi JZ, Al-Jobair MO, Al-Shwaiyat NM. Trends of fast food consumption among adolescent and young adult Saudi girls living in Riyadh. Food Nutr Res. 2015;59:26488.
19. Ruiz-de-Cenzoano M, Rochina-Marco A, López-Salazar O, Cervera ML, de la Guardia M. Mineral profile of children’s fastfood menu samples. J AOAC Int. 2017;100:1879-1884.
20. Muller P. Vegan diet in young children. Global Landscape of Nutrition Challenges in Infants and Children - 93rd Nestlé Nutrition Institute Workshop, Kolkata; 2019.
21. Lapin C, Wozniak H, Genton L, Serratrice J. Vegetarian and vegan diets and their impact on health. Rev Med Suisse. 2019;15:1849-1853.
22. Maldonado EG, Gallego-Narbón A, Vaquero MA. Are vegetarian diets nutritionally adequate? A revision of the scientific evidence. Nutr Hosp. 2019;36:950-961.

23. Cooper MJ, Cockell KA, L’Abbe MR. The iron status of Canadian adolescents and adults: current knowledge and practical implications. Can J Diet Pract Res. 2006;67:130-8.

24. Dunham L, Kollar LM. Vegetarian eating for children and adolescents. J Pediatr Health Care. 2006;20:27-34.

25. Curran CP, Marczinski CA. Taurine, caffeine, and energy drinks: Reviewing the risks to the adolescent brain. Birth Defects Res. 2017;109:1640-1648.

26. de Sanctis V, Soliman N, Soliman AT, Elsedfy H, Di Maio S, El Kholy M et al. Caffeinated energy drink consumption among adolescents and potential health consequences associated with their use: A significant public health hazard. Acta Biomed. 2017;88:222-231.

27. Musallam KM, Ali T Taher. Iron deficiency beyond erythropoiesis: should we be concerned? Curr Med Res Opin. 2018;34:81-93.

28. Kontogiorghes GJ, Kontoghiorghe CN. Iron and chelation in biochemistry and medicine: new approaches to controlling iron metabolism and treating related diseases. Cells. 2020;9:E1456.

29. Helman SL, Anderson GJ, Frazer DM. Dietary iron absorption during early postnatal life. Biometals 2019;32:385-393.

30. Hunt JR. Bioavailability of iron, zinc, and other trace minerals from vegetarian diets. Am J Clin Nutr 2003;78(suppl):633S–639S.

31. Institute of Medicine. Dietary Reference Intakes (DRIs). Available:https://www.ncbi.nlm.nih.gov/books/NBK545442/table/appJ_tab3/?report=objectonly Accessed August 28, 2020.

32. Yadav D, Chandra J. Iron deficiency: beyond anemia Indian J Pediatr. 2011;78:65–72.

33. Sherene E, Nalini G. Adolescent anemia. J Ped Nurs. 2019;7:224-227.

34. Auerbach M, Adamson JW. How we diagnose and treat iron deficiency anemia. Am J Hematol. 2018;93:31-38.

35. Camacchella C. Iron deficiency. Blood. 2019;133:30-39.

36. Cappellini MD, Musallam KM, Taher AT. Iron deficiency anaemia revisited. J Intern Med. 2020;287:153-170.

37. Hanif N, Answer F. Chronic iron deficiency In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020.

38. Ashraf T, Soliman, Vincenzo De Sanctis, Mohamed Yassin, Ashraf Adel. Growth and growth hormone – I (GH-IGF-I) axis in chronic anemias. Acta Biomed. 2017;88:101-111.

39. Clénin GE. The treatment of iron deficiency without anaemia (in otherwise healthy persons). Swiss Med Wkly. 2017;147:w14434.

40. WHO. Serum ferritin concentration for the assessment of iron status and iron deficiency in populations. Geneva; 2011.

41. Spear LP. Adolescent neurodevelopment. J Adolesc Health. 2013;52:S7-S13.

42. Erhardt J, Zagorac I. Neuroenhancement and vulnerability in adolescence. Eur J Bioeth. 2019;10:149-170.

43. Lamblim M, Murawski C, Wittle S, Fornito A. Social connectedness, mental health, and the adolescent brain. Neurosc Biobehav Rev. 2017;80:57-68.

44. Jáuregui-Lobera I. Iron deficiency and cognitive functions. Neuropsychiatr Dis Treat. 2014;10:2087-2095.

45. Agrawal S, Berggren KL, Marks E, Fox JH. Impact of high iron intake on cognition and neurodegeneration in humans and in animal models: a systematic review. Nutr Rev. 2017;75:456-470.

46. Shaw GA, Dupree JL, Neigh GN. Adolescent maturation of the prefrontal cortex: Role of stress and sex in shaping adult risk for compromisse. Genes Brain Dev. 2019:e12626. [Epub ahead of print].

47. More S, Shivkumar VB, Gangane N, Shende S. Effects of iron deficiency on cognitive function in school going adolescent females in rural area of central India. Anemia. 2013;2013:1-5.

48. Prado EL, KG. Nutrition and brain development in early life. Nutr Rev. 2014;72:267-84.

49. McCann S, Amadó MP, Moore SE. The role of iron in brain development: A systematic review. Nutrients 2020;12:E2001. [Epub ahead of print].

50. Kim J, Wessling-Resnick M. Iron and mechanisms of emotional behavior. J Nutr Biochem. 2014;25:1101-1107.
51. Młyniec K, Davies CL, Sánchez IGA, Pytka K, Bogustawa Budziszewska B, Nowak G. Essential elements in depression and anxiety. Part I. Pharmacol Rep. 2014;66:534-44.

52. Uçar HN, Koker SA, Tekin U. Irritability and perceived expressed emotion in adolescents with iron deficiency and iron deficiency anemia: a case-control study. J Ped Hematol Oncol. 2020;42:403-409.

53. Leung W, Ishmeet Singh, Scout McWilliams, Sylvia Stockler, Osman S Ipsioglu. Iron deficiency and sleep - a scoping review. Sleep Med Rev. 2020;51:101274. [Epub ahead of print].

54. Ji X, Cui N, Liu J. Neurocognitive function is associated with serum iron status in early adolescents. Biol Res Nurs. 2017;19:269-277.

55. Bailey RL, West Jr KP, Black RE. The epidemiology of global micronutrient deficiencies. Ann Nutr Metab. 2015;66(Suppl 2):22-33.

56. Mesías M, Seiquer I, Navarro MP. Iron Nutrition in Adolescence. Crit Rev Food Sci Nutr. 2013;53:1226-1237.

57. World Health Organization. Guideline: Intermittent iron and folic acid supplementation in menstruating women. World Health Organization; 2011. Available:whqlibdoc.who.int/publications/2011/9789241502023_eng.pdf

58. Nguyen M, Tadi P. Iron Supplementation. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020.