

Iron Deficiency Anemia and Pregnancy

Ines Banjari

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/intechopen.69114

Abstract

Iron deficiency is the most common nutritional deficiency in the world with immense public health consequences. It has a complex etiology and prolonged imbalance between dietary intake, absorption, and body needs which leads to iron deficiency anemia. If developed during pregnancy, it significantly alters pregnancy outcomes. Low birth weight is one of the main features, and those infants are at increased risk of developing anemia later in life. Along with widely recommended and practiced supplementation during pregnancy, proper combination of foods remain the best way for an optimal absorption of iron. Dietary iron is directly related to the total dietary energy intake, but depending on the type of its dietary source, maximum absorption is up to 40% of the total intake. Plant foods, the basis of everyday diet, contain significant number of dietary factors that inhibit iron absorption in the gut. Therefore, planning a well-balanced diet in order to achieve maximum absorption of iron from foods can be challenging. Pregnancy, especially its earliest period, is considered as the *critical window* in fetal programing, an ideal time frame to reduce risk factors for a number of health conditions in a newborn. Healthy pregnancy should be observed as a prerequisite for a healthier society.

Keywords: iron deficiency, iron deficiency anemia, iron bioavailability, pregnancy outcomes, fetal programing

1. Introduction

Iron is usually discussed from the aspect of undeveloped or developing countries that often experience food insecurity, or even famine. Deficiency of iron is the most common nutritional deficit around the globe, therefore the issue of iron is global [1, 2].

This is a multiple stage metabolic process and its main feature is gradual progression of iron deficiency (ID) toward severely depleted stores of iron in the body when iron deficiency anemia (IDA) develops. The etiology of IDA (**Figure 1**) is very complex and includes iron stores, food



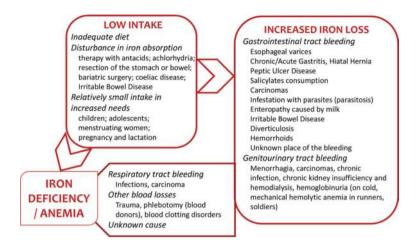


Figure 1. The etiology of iron deficiency and iron deficiency anemia (prepared according to Refs. [3, 6, 27]).

digestion, iron content, and bioavailability in foods, and iron distribution in the body through different stages in the life cycle (e.g., adolescence and pregnancy) [3-6]. In developed countries, the most common causes of IDA include genitourinary tract bleeding, fad dieting, and low consumption of iron-rich foods or foods that contain highly bioavailable iron. Additional component is economic poverty that significantly alters the quality of a person's diet [7].

However, even ID may cause loss of strength and tiredness, impaired immune response, poorer cognitive functioning, and behavior problems (social/emotional) [3, 8–13].

Pregnancy represents the critical window in child's development [14-18]. Therefore, pregnancy is considered an ideal time frame for all preventive interventions with focus put on not only iron status, but also obesity, diabetes, and other conditions.

Child's iron status reflects mother's iron status during pregnancy, and even before pregnancy. In terms of fetal programing, early pregnancy is considered extremely important [16, 19–22]. However, pregnancy outcomes, that is, fetal programing depends on numerous factors related to mother, from maternal age (the risk of adverse pregnancy outcomes increases at the age of 35 years, especially in the case of the first pregnancy), maternal state of nourishment (overweight and obesity significantly alters pregnancy outcomes), diabetes or gestational diabetes, and maternal weight gain during gestation [14]. Proper and specifically timed nutritional intervention could significantly reduce the risk of adverse pregnancy outcomes [19, 20].

From the aspect of iron status, it is important to note that a significant proportion of women start pregnancy with depleted iron stores [2, 23, 24]. In the United States, more than one-third of women of reproductive age have deprived iron stores [3]. Additionally, all women having ID are at the risk of developing IDA early in the course of gestation [1, 21, 25]. Requirements for iron increase significantly during pregnancy, so if not recognized and treated may cause adverse pregnancy outcomes, especially for a newborn. Adverse pregnancy outcomes include

low birth weight infants, preterm delivery, labor complications, and higher rates of cesarean section [23, 24, 26–30]. The risk increases with the more severe stages of ID [21, 23, 24, 26, 27, 29]. A newborn enters an infinite loop of ID and its related health problems [31].

All stated additionally highlights the importance of proper food combination during pregnancy [32]. Timed recognition and proper treatment of ID could significantly alter health indicators, not only on an individual level but also on a population level. The more recent findings shed a new light on ID which favors the proposed idea; obesity has been linked to low iron stores, confirmed in both pregnant women and children [20, 33–37].

2. Definitions and prevalence

Prevalence around the world varies widely. According to the World Health Organization (WHO), the frequency of ID in developing countries is about 2.5 times that of anemia [1]. However, Croatia ID is 3.8 times more frequent among pregnant women at early pregnancy [25], which backs up the theory of depleted iron stores before pregnancy [3]. The incidence is high especially during pregnancy and lactation in both, industrialized and developing countries [2, 38]. Estimated prevalence of anemia is 43% in nonpregnant women in developing countries and 12% in wealthier regions [1]. On the other hand, estimates from the WHO report indicate that anywhere between 35 and 75% (56% on average) of pregnant women in developing countries and 18% of pregnant women from industrialized countries are ID, with half of them having IDA [1].

During pregnancy, maternal iron stores should be sufficient to maintain homeostasis of iron for the normal growth and development of fetus. Still, as pregnancy progresses physiologic anemia in later phases can be expected, due to hemodilution, a process of nonsimultaneous and disproportional increase in the total plasma volume (the total increase of around 50%, caused by aldosterone and estrogen) and the number of erythrocytes (the total increase of around 33%; erythropoiesis) [3–6, 21]. Moreover, physiology of pregnancy requires additional 800 mg of circulating iron during gestation [3, 6, 39, 40]. Therefore, ID and IDA often develop during the later stages of pregnancy even in women who enter pregnancy with relatively adequate iron stores [21, 23].

The WHO defines anemia as hemoglobin level below 110 g/l for pregnant women, or hematocrit level below 0.330 l/l [1, 41]. This criterion has been widely argued for its low sensitivity toward less severe stages of IDA [25, 30, 40, 42]. Therefore, clinical interpretation is useless unless iron-binding capacity values, that is, transferrin saturation percentage, are available at the same time [40, 42]. In IDA unsaturated-iron binding capacity (UIBC) and total iron-binding capacity (TIBC) are increased while usually transferrin saturation, which normally ranges between 20 and 50%, drops below 15.0%. So, for screening purpose and clinical decision, the WHO besides hemoglobin and hematocrit recommends either serum ferritin or transferrin saturation [1, 41, 42].

In Croatia, based on the WHO criteria, 17.7% (on hemoglobin basis) and 18.5% (on hematocrit basis) of pregnant women in early pregnancy had either ID or IDA. Clinical criteria showed

that even 32.8% of pregnant women in early pregnancy had either ID or IDA (transferrin saturation <20.0%) [25]. The data support the global significance of proper iron stores among women and ID problem in developed countries.

3. Iron bioavailability

Various food sources have different amounts of bioavailable iron, that is, the amount of iron that can readily be absorbed in duodenum [6]. Still, a significant number of diet-related factors affect the final amount of iron available for the absorption.

For the iron absorption acidity in the stomach is very important (**Figure 2**). Absorption of nonheme iron is limited to duodenum [6]. Nonheme iron is presented in one of the two forms: ferric (Fe^{3+}) or ferrous (Fe^{2+}) form. The ferric form tends to form complex salts with anions and asks for a very low pH in the stomach (below 3). On the other hand, ferrous iron is soluble up to pH 8 [6, 43].

Iron in foods is present as heme and nonheme, deferring by solubility, sources, and absorption level [6]. Foods that are part of the usual, everyday meals have low iron content and low bioavailability. So, only 10–20% of the total iron intake is absorbed, but the absorption percentage is higher if IDA is present [1, 2, 44, 45]. The reason for low absorption lies in numerous inhibitors of iron absorption, such as phytic and oxalic acid, starch, polyphenols (i.e., tannins

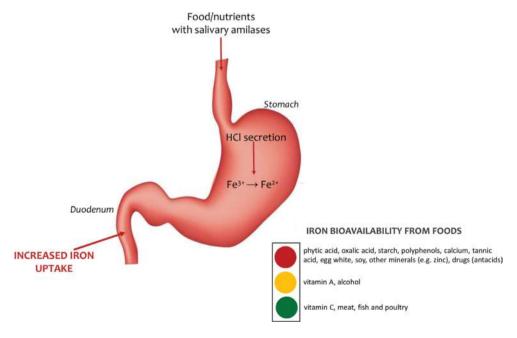


Figure 2. Parts of the gastrointestinal system important for the digestion and absorption of iron from foods and supplements.

from coffee and tea), egg white, calcium, other minerals (e.g., zinc), and numerous medicaments that diminish gastric secretion (e.g., antacids) [2, 32, 46-49].

Dietary intake of iron directly correlates with energy intake (on every 4184 kJ comes about 6 mg of iron) [3, 6, 39, 40]. Recommended intake (presented as dietary reference intakes (DRI) [50]) for pregnant women along with percentage increase from nonpregnant women recommendations is given in Table 1. Out of all micronutrients, iron and folic acid requirements increase by 50.0% in comparison to nonpregnant women. Folic acid role in pregnancy extends the scope of this chapter. For further details please refer to, for example, Banjari et al. [15].

Generally speaking, a well-balanced diet goes hand-in-hand with iron-rich foods. But, despite general belief of positive shifts in diet quality during pregnancy [51, 52], pregnant women do not change it significantly through pregnancy [4, 32]. However, changes in lifestyle habits are reflected in smoking cessation and supplement use, but not in diet quality [4, 32]. Educative programs for pregnant women could significantly alter their behavior, especially in terms of diet and not only during pregnancy but on a long-term basis [53–56].

Dietary intervention has shown to improve the iron status of pregnant women gradually and provides better results long-term [53, 55, 56]. Patterson et al. [56] conducted a 12-week intervention, with a follow-up 6 months after the intervention on ID and IDA pregnant women with either iron supplement or iron-rich diet. The supplement group took one tablet containing 350 mg of slow-release ferrous sulfate tablet per day, which was equivalent to 105 mg inorganic iron. On the other hand, the iron-rich diet group followed a diet planned to provide approximately 2.25 mg of absorbed iron per day. Both groups showed significant improvement in serum ferritin levels after the intervention and at follow-up. However, the increase was smaller in the diet group which continually improved iron

Nutrient	DRI	% increase	Nutrient	DRI	% increase
CHO (g/d)	175	34.6	Folate (µg/d)	600	50.0
Total fiber (g/d)	28	12.0	$B_{12} (\mu g/d)$	2.6	8.3
Protein (g/d)	71	54.0	Pantothenic acid (mg/d)	6	20.0
Vitamin A (μg/d)	770	10.0	Biotin (µg/d)	30	0.0
Vitamin C (mg/d)	85	13.3	Sodium (g/d)	2.3	0.0
Vitamin D (μg/d)	5	0.0	Ca (mg/d)	1000	0.0
Vitamin E (mg/d)	15	0.0	Cu (µg/d)	1000	11.1
Vitamin K (μg/d)	90	0.0	Fe (mg/d)	27	50.0
$B_1 (mg/d)$	1.4	27.3	Mg (mg/d)	350-360	10.9
$B_2 (mg/d)$	1.4	27.3	Mn (mg/d)	2.0	11.1
Niacin (mg/d)	18	28.6	Se (µg/d)	60	9.1
$B_6 (mg/d)$	1.9	46.2	Zn (mg/d)	11	37.5

Table 1. Dietary reference intakes (DRIs) for pregnant women (prepared according to IOM [50]).

status during 6 months follow-up [56]. These results clearly show the potential of properly balanced iron-rich diet as a mean for the improvement in iron status, and if timed properly present the best way to prevent ID and IDA in pregnancy.

The total dietary intake of iron increases significantly through gestation [28, 32, 38, 47, 52], reaching the highest peak at the third trimester [32]. Still, this amount is significantly under the recommended intake [50] and as reported by Banjari et al. [32], the total daily dietary intake of iron in pregnant women satisfies 35.2% in the first trimester, 37.4% in the second trimester, and increasing to 41.5% in the third trimester of the recommended DRI of iron. Shobeiri et al. [28] reported the intake of iron in Indian pregnant women to around 60% of DRI. On the other hand, even with relatively low total dietary intake of iron proper combination of foods may significantly improve the amount of iron absorbed [32, 56].

The presence of ID or IDA increases the amount of dietary iron which will be readily absorbed in the gut [2, 3, 6]. Barett et al. [57] have shown that the iron absorption increases through pregnancy, which is foreseeable as a normal physiologic process in pregnancy. Therefore, the iron absorption reaches its maximum by the end of gestation. In other words, the absorption of the total dietary iron starts with 7% absorbed in the first trimester, 36% in the second, and increases to 66% of absorbed iron in the third trimester, falling again postpartum to starting level (of around 11%) [57]. Banjari et al. [32] also confirmed that the amount of absorbed iron follows rising trend toward the end of pregnancy, being the highest in the third trimester being 1.33 mg of absorbed iron (out of 11.2 mg of total dietary iron intake) [32].

Banjari et al. [32] explained this low level of absorbed iron by the fact that plant foods present the main source of dietary iron for pregnant women, contributing more than 80% to the total dietary intake of iron [32]. Plant foods have been confirmed by numerous studies [2, 47–49, 56, 58, 59] to represent the main dietary source of iron for pregnant women.

Another possible reason includes low intake of meat; Banjari et al. [32] reported daily intake of meat to around 90 g a day. Therefore, the contribution of heme iron to the total dietary intake of iron is low, varying from 15.8, 16.4, and 16.6%, respectively, through gestation [32]. One of the main reasons is high consumption of chicken meat [32], which does not contain heme iron [60]. In the past two decades, consumption of poultry increased by 50% while simultaneously beef consumption fell by 40%; therefore, the amount of heme iron consumption is significantly lower [59]. Still, the so-called *meat factor* effect as well as amino acids with sulfur show positive influence on iron absorption [46, 61].

Consumption of cereals is very important part of a well-balanced diet. However, due to high content of phytates, one of the most potent inhibiting factors for iron bioavailability [46, 62] must be considered with special care, especially in countries with high consumption of cereals and cereal products [63–65]. According to Johnston et al. [59], cereals present the most important contributing source to overall intake of nonheme iron. These foods are the main source of the most potent inhibiting absorption factor, phytates [46, 62], which have been shown to correlate significantly with hemoglobin values of pregnant women, only in the first trimester of pregnancy [4]. This correlation points out that physiology of pregnancy diminishes the effect of inhibition by phytates as pregnancy progresses. Cereals and their products may be

used as highly valuable foods by which an individual could increase the total daily dietary iron intake [48, 63] and have been used as functional foods, that is, foods enriched with iron either by a biofortification method or addition of different iron compounds (e.g., electrolytic iron, ferrous fumarate, ferrous pyrophosphate, ferrous lactate, etc.) [48]. Interventions based on iron fortification resulted in a significant drop of ID and IDA prevalence in countries, such as China, Brazil, Venezuela, Morocco, and others [48]. In addition, potential adverse effects of high intake of iron must be considered [6], but never the less, functional cereal products enriched with iron could serve as a good basis to improve the total dietary intake of iron of not only pregnant women, but also menstruating women and children, that is, population groups at the risk of insufficient intake of iron [63, 66].

Consumption of coffee and tea are additional important factors due to wide consumption on a daily basis [4, 67]. According to a prospective study conducted in Denmark between 1989 and 1996 on 18,478 singleton pregnancies, 43% of women did not drink coffee, 34% drank one to three cups a day, with 23% of women categorized as heavy users with four or more cups a day [68]. The results from the Danish National Birth Cohort covering time frame between 1996 and 2002 showed 81.2% of women reported drinking either tea or coffee, with coffee being consumed less (44.7% of women) than tea (63.5% of women), and with the average consumption of two cups per day [69]. The results from the Slone Epidemiology Center Birth Defects Study [70], which covered three periods, that is, 1976–1988, 1998–2005, and 2009–2010, show that tea drinking was more popular in early years with 66% of pregnant women consuming tea, which dropped to 39% in later years. On the other hand, a prospective study by Banjari et al. [67] reports that 68.9% of pregnant women were drinking either coffee, tea, or both during pregnancy, with the highest preference toward coffee (130 out of 153 women). The inhibiting effect of coffee and tea is related to polyphenols (garlic, tannic, and chlorogenic acid). Tea shows higher reduction rate (75-80% for cca 200 ml) than the coffee (by 60% for cca 150 ml). Moreover, the consumption of around 100 g of meat reduces their inhibiting effect by 50% [46, 71, 72]. However, it should be noted that pregnant women tend to cease from their preferred beverage due to nausea or heartburn. Heartburn is experienced by 40-80% of pregnant women sometime during pregnancy, while nausea affects nearly 80-90% of pregnant women followed by vomiting in 50% cases [73]. As reported by Banjari et al. [67], during the first trimester 17.0% of women gave up their preferred beverage due to nausea, while at the third trimester additional 17.7% of coffee drinkers and 26.1% of tea drinkers stopped drinking a particular beverage, referring heartburn as a reason.

Intake of calcium higher than 600 mg/day was found to have the maximum inhibiting effect on iron absorption [46, 74–76]. However, we must emphasize that in terms of a newborn prolonged breastfeeding serves as a protecting agent from IDA [31].

Child's diet especially in that early period solely depends on the mother [31]. Strong evidence supports findings that in both low- and high-income settings omission from breastfeeding contributes to infant mortality, hospitalization for preventable disease, such as gastroenteritis and respiratory disease, increased rates of childhood diabetes and obesity, and adult disease, such as coeliac and cardiovascular disease [77]. Breastfeeding impacts IQ and educational and behavioral outcomes of the child. Importantly, a dose-response relationship was found with

the greatest benefit resulting from breastfeeding exclusively, with no added food or fluids, for around 6 months [77], which has been recommended by the WHO [78]. Race and income are major predictors of whether women will exclusively breastfeed for 6 months. The highest rate of breastfeeding is among wealthy whites [77, 78]. However, women with low incomes are often financially compelled to quickly return to the workforce [7], and for them formula is a convenience. But in a time of prolonged economic poverty child's dietary patterns worsen, and mothers even return to earlier practice of giving cow's milk which worsens the symptoms of IDA [3, 6, 31, 74].

On the other hand, intake of vitamin C (ascorbic acid) which has the most promoting effect on iron absorption is especially effective when the most powerful inhibitors are present in a meal [46, 79]. Besides important correlation with the gastric acidity [79], which has immense importance for the overall absorption of iron (**Figure 2**), ascorbic acid prevents the formation of low soluble ferric compounds by a reduction process [46] and this important promoting effect has been observed with or without the presence of phytates [80] or polyphenols [46]. The promoting effect of ascorbic acid depends on the meal composition [81].

Besides already discussed inhibiting and promoting factors, two factors have combined effect on iron absorption. Alcohol increases the absorption of ferric but not of ferrous iron, and this effect has been attributed to enhanced gastric acid secretion [46]. However, the effect was not found in red wine, probably due to high polyphenol content [46, 72]. Vitamin A reduces the inhibiting effect of tea or coffee, that is, it overcomes the inhibiting effect of polyphenols in these beverages, as well as the effect by phytates. They form a complex which is soluble even at pH 6, making iron available for absorption in duodenum. An even stronger effect was found for beta-carotene and other carotenoids (lycopene, lutein, and zeaxanthin) [4].

4. Supplementation and other lifestyle habits

Supplementation in pregnancy is highly recommended [2, 24, 38] because of the already mentioned increased needs (**Table 1**), and low dietary intake [28, 32, 38, 51, 52]. Supplementation with iron or iron-folic acid has been widely recommended and practiced [4, 21]; in Croatia, even 82.6% of pregnant women were taking supplements during pregnancy [4]. Still, general supplementation should be avoided [82] especially having in mind that the recent systematic review and meta-analysis conducted by Fernández-Cao et al. [22] found almost 50% increased risk of gestational diabetes in women having high hemoglobin or ferritin levels, especially in the first and the third trimesters. Additionally, supplements formulated specifically for pregnant women differ significantly in their composition, and if only iron is observed, the intake from producer's prescribed dose (1 or 2 tablets per day) varies from 8 mg up to even 60 mg of iron [4]. Findings from clinical trials on how different supplementation formulations affect iron status during pregnancy and pregnancy outcomes (i.e., time of delivery and birth weight) are equivocal. For example, West et al. [83] conducted a cluster randomized, double-masked trial enrolling more than 44,000 pregnant women from rural Bangladesh who were provided with supplements containing 15 micronutrients or iron-folic acid alone. Multiple

micronutrient supplementation group had statistically significant reduction in preterm delivery (RR 0.85, P = 0.02) and low birth weight (RR 0.88, P < 0.001) as compared to iron-folic acid supplementation group [83]. This contradicts earlier findings from a double-masked randomized controlled community trial conducted on pregnant women from rural Nepal [84]. Study results showed that supplementation with iron-folic acid had increased hemoglobin and had a 54% reduction in IDA; the combination of folic acid, zinc, and iron had a 48% reduction, while the combination of folic acid, zinc, iron, and 11 other micronutrients had a 36% reduction, whereas supplementation with folic acid alone had no influence on IDA [84]. The more recent meta-analysis performed by Petry et al. [85] found that supplementation with iron or zinc during pregnancy had no effect on birth outcomes, but did show the positive effect of low dose daily iron and zinc use during 6-23 months of age on child's iron and zinc status, especially weight-for-age and weight-for-height [85]. Supplementation is encouraged due to expected improvement in iron blood status. A study by Scanlon et al. [29] showed that the prevalence of anemia (based on hemoglobin level) among iron-supplemented pregnant women participating in public health nutrition programs is approximately 8% in the first trimester, but this was not confirmed by Banjari [4] reporting that 3.6% of pregnant women were IDA with additional 10.8% being ID at the first trimester.

One of the most detrimental lifestyle habits during pregnancy is smoking. It has been associated with the increased risk for spontaneous abortion, especially during the first trimester, reduced birth weight, and perinatal mortality [86, 87]. In combination with ID and especially IDA negative effect on pregnancy outcomes is even greater, leading toward low birth weight and preterm delivery [86, 87]. Smoking cessation is very common among pregnant women, and as reported by Banjari [4] even 72.8% of pregnant women decided to stop smoking during pregnancy, while 27.2% of women continue to smoke regardless of all recommendations and the knowledge of its adverse impact on child's health.

5. ID, IDA poverty, and obesity

Iron-rich foods and those that contain nutrients that promote iron absorption fall into a group of foods with the highest price per serving [88]. According to the Food and Drug Administration "healthy foods" are defined as foods based on the protein, fiber, vitamins A and C, calcium, and iron content, and cost analysis showed that grains, dry beans, and eggs are the lowest cost sources of iron [89]. However, those foods contain iron of very low bioavailability [32, 46]. A well-balanced diet with highly bioavailable iron must include foods like meat, fish, and fruits. It is estimated that around one-third of children have low dietary intake of iron [90]. At the time of economic insecurity and fall in socioeconomic status (SES), these foods are the first ones being cut from a diet [91].

At first, the link between iron deficiency and obesity seems farcical. However, in the obesity pandemic era [92], we are experiencing micronutrient deficiencies that are not expected in developed, rich countries [20, 33–35]. The trend affects all population groups; therefore, it is no surprise that overweight/obesity condition is considered the number one priority

currently in obstetrics and gynecology [19]. In Croatia, as reported by Banjari [4], 16.7% women start pregnancy as overweight, with additional 10.3% being obese. If we add up excessive weight gain during pregnancy, which was observed among 40.5% of all pregnant women in Croatia [4], the impact of obesity on pregnancy outcomes and future child's health is immense.

The preexistence of overweight/obesity or excessive weight gain during pregnancy represents a significant risk factor for fetal macrosomia and medical complications, including pregnancy-induced hypertension, gestational diabetes, and cesarean delivery [19, 20, 93–99]. Importantly, for women entering pregnancy with a normal body mass index, an inadequate weight gain poses higher risk [20, 94, 95, 100]. Besides, maternal obesity and gestational weight gain are confirmed risk factors for childhood obesity [98, 101], with effects that extend into adulthood [98, 99, 102]. No wonder why childhood obesity rates and predictions seem especially alarming. The predictions say that by 2025 the rate of overweight children is expected to increase to 15.8%, with additional 5.4% of obese children aged 5–18 years by 2025 [103].

A systematic review by Zhao et al. [37] confirmed a significant correlation between ID (including the risk of ID) in obese and overweight individuals. Obese individuals despite their excessive dietary and caloric intake have an unbalanced diet based on carbohydrates and fats [35]. This has also been confirmed for overweight and obese children by Hutchinson [36]. This systematic review concluded that overweight and obese children and adolescents have a higher prevalence or risk of ID, and the evidence is consistent. However, Hutchinson [36] emphasized that the true relationship between body fat mass and iron absorption is still to be clarified. Low-hemoglobin level was found among overweight/obese pregnant women [19].

As already mentioned, pregnancy is observed as a *critical window* for future child's development and considered as an ideal time frame for interventions that would target specific health-related outcomes in child, such as obesity, diabetes, etc. [14, 16, 98, 99, 104]. Evidence supporting this approach accumulates by day. There is no such pretimed intervention, and as nicely emphasized by Gillman and Ludwig [99] *timely intervention during the early, plastic phases of development may lead to improved lifelong health trajectories*.

To sum up on the relation between obesity and ID/IDA, both conditions are more prevalent in population groups with low-quality diet. The relation extends beyond low-SES, consumption of low-cost foods that generally have a low content of essential nutrients [35, 105, 106], and especially iron [88]. Additionally, for pregnant women characteristics, such as younger age, lower level of education, with more children, and with higher prepregnancy, body mass index significantly alters diet quality during pregnancy [20, 51, 52]. In other words, this is an infinite loop of ID and IDA [31]. Therefore, targeting pregnant women affected by any of the above-mentioned characteristics/risk factors could significantly improve not only their iron status but also their state of nourishment and the overall health status. By that, we would alter future generations of children, making it a prerequisite for a healthier society.

Author details

Ines Banjari

Address all correspondence to: ines.banjari@ptfos.hr

Faculty of Food Technology Osijek, University of Osijek, Osijek, Croatia

References

- [1] WHO/UNICEF/UNU. Iron deficiency anaemia: Assessment, prevention, and control. Geneva (Switzerland): World Health Organization; 2001
- [2] Zimmermann MB, Hurrell RF. Nutritional iron deficiency. Lancet. 2007;370:511-520
- [3] Adamson JW. Iron deficiency and other hypoproliferative anemias. In: Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, Loscalzo J, editors. Harrison's Principles of Internal Medicine. 17th ed. New York: Mc-Graw Hill Medical; 2008. pp. 628-634
- [4] Banjari I. Dietary intake and iron status and incidence of anaemia in pregnancy [thesis]. Zagreb: University of Zagreb; 2012
- [5] Heidemann BH. Changes in maternal physiology during pregnancy. Update in Anaesthesia. 2005;20:21-24
- [6] Boulpaep EL, Boron W F. Medical Physiology. Philadelphia, PA: Elsevier, Saunders; 2006. p. 1267. ISBN 978-1-4160-3115-4
- [7] Drewnowski A, Eichelsdoerfer P. Can low-income Americans afford a healthy diet? Nutrition Today. 2010;44(6):246-249
- [8] Chepelev NL, Willmore WG. Regulation of iron pathways in response to hypoxia. Free Radical Biology & Medicine. 2011;50:645-666
- [9] Cairo G, Bernuzzi F, Recalcati S. A precious metal: Iron, an essential nutrient for all cells. Genes & Nutrition. 2006;1(1):25-40
- [10] Lozoff B, Georgieff MK. Iron deficiency and brain development. Seminars in Pediatric Neurology. 2006;13:158-165
- [11] Zhou SJ, Gibson RA, Crowther CA, Baghurst P, Makrides M. Effect of iron supplementation during pregnancy on the intelligence quotient and behavior of children at 4 y of age: Long-term follow-up of a randomized controlled trial. The American Journal of Clinical Nutrition. 2006;83:1112-1117
- [12] Hulthén L. Iron deficiency and cognition. Scandinavian Journal of Nutrition. 2003;47(3): 152-156

- [13] Grantham-McGregor S, Ani C. A review of studies on the effect of iron deficiency on cognitive development in children. Journal of Nutrition. 2001;131:649S-668S
- [14] Banjari I. Healthy pregnancy as a foundation for healthy child. Journal of Society of Medical Doctors of Montenegro Medical Essays. 2016;65(Suppl 1):88-98
- [15] Banjari I, Matoković V, Škoro V. The question is whether intake of folic acid from diet alone during pregnancy is sufficient. Medicinski Pregled. 2014;67(9-10):313-321
- [16] Langley-Evans SC. Metabolic programming during pregnancy: Implications for personalized nutrition. In: Kok F, Bouwman L, Desire F, editors. Personalized Nutrition. Principles and Applications. Routledge: CRC Press; 2008. p. 101-114
- [17] Gambling L, Dunford S, Wallace DI, Zuur G, Solanky N, Srai SKS, McArdle HJ. Iron deficiency during pregnancy affects post-natal blood pressure in the rat. The Journal of Physiology. 2003;52(2):603-610
- [18] Godfrey KM, Forrester T, Barker DJ, Jackson AA, Landman JP, Hall JS, Cox V, Osmond C. Maternal nutritional status in pregnancy and blood pressure in childhood. British Journal of Obstetrics and Gynaecology. 1994;101(5):398-403
- [19] Banjari I, Kenjerić D, Šolić K, Mandić ML. Cluster analysis as a prediction tool for pregnancy outcomes. Collegium Antropologicum. 2015;1:247-252
- [20] Banjari I, Kenjerić D, Mandić ML, Glavaš M, Leko J. Longitudinal observational study on diet quality during pregnancy and its relation to several risk factors for pregnancy complications and outcomes. British Journal of Medicine & Medical Research. 2015;7(2):145-154. DOI: 10.9734/BJMMR/2015/15527
- [21] Scholl TO. Maternal iron status: Relation to fetal growth, length of gestation, and iron endowment of the neonate. Nutrition Reviews. 2011;69(Suppl 1):S23-S29
- [22] Fernández-Cao JC, Aranda N, Ribot B, Tous M, Arija V. Elevated iron status and risk of gestational diabetes mellitus: A systematic review and meta-analysis. Maternal & Child Nutrition. 2016; DOI: 10.1111/mcn.12400
- [23] Allen LH. Anemia and iron deficiency: Effects on pregnancy outcome. The American Journal of Clinical Nutrition. 2000;71(Suppl):1280S-1284S
- [24] Milman N, Bergholt T, Eriksen L, Byg K-E, Graudal N, Pedersen P, Hertz J. Iron prophylaxis during pregnancy—How much iron is needed? A randomized dose-response study of 20-80 mg ferrous iron daily in pregnant women. Acta Obstetricia et Gynecologica Scandinavica. 2005;84:238-247
- [25] Banjari I, Kenjerić D, Mandić M. What is the real public health significance of iron deficiency and iron deficiency anaemia in croatia? A population-based observational study on pregnant women at early pregnancy from eastern Croatia. Central European Journal of Public Health. 2015;23(2):122-127
- [26] Levy A, Fraser D, Katz M, Mazor M, Sheiner E. Maternal anemia during pregnancy is an independent risk factor for low birth weight and preterm delivery. European Journal of Obstetrics Gynecology and Reproductive Biology. 2005;122:182-186

- [27] Scholl TO, Hedinger ML, Fischer RL, Shearer JW. Anemia vs iron deficiency: Increased risk of preterm delivery in a prospective study. The American Journal of Clinical Nutrition. 1992;55:985-988
- [28] Shobeiri F, Begum K, Nazari M. A prospective study of maternal hemoglobin status of Indian women during pregnancy and pregnancy outcome. Nutrition Research. 2006;26: 209-213
- [29] Scanlon KS, Yip R, Schieve LA, Cogswell ME. High and low hemoglobin levels during pregnancy: Differential risks for preterm birth and small for gestational age. Obstetrics & Gynecology. 2000;96(5):741-748
- [30] Viteri FE, Berger J. Importance of pre-pregnancy and pregnancy iron status: Can long-term weekly preventive iron and folic acid supplementation achieve desirable and safe status? Nutrition Reviews. 2005;63(12):S65-S76
- [31] Banjari I. A maternal bond: The story on the infinite loop of iron deficiency anaemia. Medicinski Pregled. 2015;68(5-6):211-212
- [32] Banjari I, Kenjerić D, Mandić ML. Iron bioavailability in daily meals of pregnant women. Journal of Food and Nutrition Research. 2013;52:203-209
- [33] Nead KG, Halterman JS, Kaczorowski JM, Auinger P, Weitzman M. Overweight children and adolescents: A risk group for iron deficiency. Pediatrics. 2004;114(1):104-108
- [34] Turer CB, Lin H, Flores G. Prevalence of vitamin D deficiency among overweight and obese US children. Pediatrics. 2013;131(1):e152-e161
- [35] Pinhas-Hamiel O, Newfield RS, Koren I, Agmon A, Lilos P, Phillip M. Greater prevalence of iron deficiency in overweight and obese children and adolescents. International Journal of Obesity and Related Metabolic Disorders. 2003;27(3):416-418
- [36] Hutchinson C. A review of iron studies in overweight and obese children and adolescents: A double burden in the young? European Journal of Nutrition. 2016;55(7):2179-2197
- [37] Zhao L, Zhang X, Shen Y, Fang X, Wang Y, Wang F. Obesity and iron deficiency: A quantitative meta-analysis. Obesity Reviews. 2015;16(12):1081-1093
- [38] Lee J-I, Kang SA, Kim S-K, Lim H-S. A cross sectional study of maternal iron status of Korean women during pregnancy. Nutrition Research. 2002;22:1377-1388
- [39] Berger J, Wieringa FT, Lacroux A, Dijkhuizen MA. Strategies to prevent iron deficiency and improve reproductive health. Nutrition Reviews. 2011;69:S78–S86
- [40] Wheeler S. Assessment and interpretation of micronutrient status during pregnancy: Symposium on translation of research in nutrition II: The bed. Proceedings of the Nutrition Society;2008;67:437-450. https://www.cambridge.org/core/services/aop-cambridge-core/content/view/S0029665108008732
- [41] World Health Organization. Assessing the iron status of populations. Geneva (Switzerland): World Health Organization, Department of Nutrition for Health and Development; 2004

- [42] Cook J. Diagnosis and management of iron-deficiency anaemia. Best Practice & Research Clinical Haematology. 2005;18(2):319-332
- [43] Lynch SR. Interaction of iron with other nutrients. Nutrition Reviews. 1997;55(4):102-110
- [44] Hurrell R, Egli I. Optimizing the bioavailability of iron compounds for food fortification. In: Kraemer K, Zimmermann MB, editors. Nutritional Anemia. Basel: Sight and Life Press; 2007. pp. 77-97
- [45] Human vitamin and mineral requirements. Report of a joint FAO/WHO expert consultation Bangkok, Thailand. Rome: Food and Nutrition Division FAO; 2001. p. 286
- [46] Hallberg L, Hultén L. Prediction of dietary iron absorption: An algorithm for calculating absorption and bioavailability of dietary iron. The American Journal of Clinical Nutrition. 2000;71:1147-1160
- [47] Milman N. Iron in pregnancy—A delicate balance. Annals of Hematology. 2006;85(9): 559-565
- [48] Thompson B. Food-based approaches for combating iron deficiency. In: Kraemer K, Zimmermann MB, editors. Nutritional Anemia. Basel: Sight and Life Press; 2007. pp. 337-358
- [49] Tapiero H, Gaté L, Tew KD. Iron: Deficiencies and requirements. Biomedicine & Pharmacotherapy. 2001;55(6):324-332
- [50] Institute of Medicine. Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein and Amino Acids. Washington, DC: National Academy Press; 2002
- [51] Rifas-Shiman SL, Rich-Edwards JW, Kleinman KP, Oken E, Gillman MW. Dietary quality during pregnancy varies by maternal characteristics in project Viva: A US cohort. Journal of the American Dietetic Association. 2009;109(6):1004-1011
- [52] Petrakos G, Panagopoulos P, Koutras I, Kazis A, Panagiotakos D, Economou A, Kanellopoulos N, Salamalekis E, Zabelas A. A comparison of the dietary and total intake of micronutrients in a group of pregnant Greek women with the dietary reference intakes. European Journal of Obstetrics Gynecology and Reproductive Biology. 2006;127:166-171
- [53] Viteri FE. Iron endowment at birth: Maternal iron status and other influences. Nutrition Reviews. 2011;69:S3-S16
- [54] Verbeke W, De Bourdeaudhuij I. Dietary behaviour of pregnant versus non-pregnant women. Appetite. 2007;48:78-86
- [55] Black MM, Quigg AM, Hurley KM, Reese Pepper M. Iron deficiency and iron-deficiency anemia in the first two years of life: Strategies to prevent loss of developmental potential. Nutrition Reviews. 2011;69:S64-S70
- [56] Patterson AJ, Brown WJ, Roberts DCK, Seldon MR. Dietary treatment of iron deficiency in women of childbearing age. The American Journal of Clinical Nutrition. 2001;74:650-656

- [57] Barett JFR, Whittaker PG, Williams JG, Lind T. Absorption of non-haem iron from food during normal pregnancy. British Medical Journal. 1994;309:79-82
- [58] Hoppe M, Sjöberg A, Hallberg L, Hulthén L. Iron status in Swedish teenage girls: Impact of low dietary iron bioavailability. Nutrition. 2008;24:638-645
- [59] Johnston J, Prynne CJ, Stephen AM, Wadsworth MEJ. Haem and non-haem iron intake through 17 years of adult life of a British Birth Cohort. British Journal of Nutrition. 2007;98(5):1021-1028
- [60] Hallberg L, Hultén L. Perspectives on iron absorption. Blood Cells, Molecules and Diseases. 2002;29(3):562-573
- [61] Reddy MB, Hurrell RF, Cook JD. Meat consumption in a varied diet marginally influences nonheme iron absorption in normal individuals. Journal of Nutrition. 2006;136(3):576-581
- [62] Kristensen MB, Tetens I, Alstrup Jørgensen AB, Dal Thomsen A, Milman N, Hels O, Sandström B, Hansen M. A decrease in iron status in young healthy women after longterm daily consumption of the recommended intake of fibre-rich wheat bread. European Journal of Nutrition. 2005;44(6):334-340
- [63] Banjari I, Kenjerić D, Mandić ML. Cereals and their products as source of energy and nutrients in early pregnancy. In: Proceedings of the 6th International Congress FLOUR-BREAD'11. Osijek, Croatia: Faculty of Food Technology Osijek; 2012. pp. 110-117
- [64] Cecić I, Colić Barić I, Kuvačić S, Batinić M. Diet quality and grains intake in Croatian pregnant women. In: Proceedings of the 5th International Congress Flour-Bread '09. Osijek, Croatia: Faculty of Food Technology Osijek; 2010. pp. 463-470
- [65] Snook Parrott M, Bodnar LM, Simhan HN, Harger G, Markovic N, Roberts JM. Maternal cereal consumption and adequacy of micronutrient intake in the periconceptional period. Public Health Nutrition. 2008;12(8):1276-1283
- [66] Miler JL. Iron Deficiency Anemia: A Common and Curable Disease. Cold Spring Harbor Perspectives in Medicine. 2013;3(7):a011866. DOI: 10.1101/cshperspect.a011866
- [67] Banjari I, Kenjerić D, Mandić ML. Intake of tannic acid from tea and coffee as a risk factor for low iron bioavailability in pregnant women. Food in Health and Disease. 2013;2(1):10-16
- [68] Wisborg K, Kesmodel U, Bech BH, Hedegaard M, Henriksen TB. Maternal consumption of coffee during pregnancy and stillbirth and infant death in first year of life: Prospective study. British Medical Journal. 2003;326:420
- [69] Hinkle SN, Laughon SK, Catov JM, Olsen J, Bech BH. First trimester coffee and tea intake and risk of gestational diabetes mellitus: A study within a national birth cohort. An International Journal of Obstetrics and Gynaecology. 2014;122(3):420-428. DOI: 10.1111/1471-0528.12930
- [70] Yazdy MM, Tinker SC, Mitchell AA, Demmer LA, Werler MM. Maternal tea consumption during early pregnancy and the risk of spina bifida. Birth Defects Research Part A Clinical and Molecular Teratology. 2012;94(10):756-761. DOI: 10.1002/bdra.23025

- [71] Hurrell RF, Reddy M, Cook JD. Inhibition of non-haem iron absorption in man by polyphenolic-containing beverages. British Journal of Nutrition. 1999;81(4):289-295
- [72] Manach C, Scalbert A, Morand C, Rémésy C, Jiménez L. Polyphenols: Food sources and bioavailability. The American Journal of Clinical Nutrition. 2004;79(5):727-747
- [73] Keller J, Frederking D, Layer P. The spectrum and treatment of gastrointestinal disorders during pregnancy. Nature Clinical Practice Gastroenterology & Hepatology. 2008;5(8):430-443. DOI: 10.1038/ncpgasthep1197
- [74] Ziegler EE. Consumption of cow's milk as a cause of iron deficiency in infants and toddlers. Nutrition Reviews. 2011;69:S37-S42
- [75] Lynch SR. The effect of calcium on iron absorption. Nutrition Research Reviews. 2000;13: 141-158
- [76] Gleerup A, Rossander-Hulthen L, Gramatkovski E, Hallberg L. Iron absorption from the whole diet: Comparison of the effect of two different distributions of daily calcium intake. The American Journal of Clinical Nutrition. 1995;61:97-104
- [77] Renfrew MJ, McCormick FM, Wade A, Quinn B, Dowswell T. Support for healthy breast-feeding mothers with healthy term babies. Cochrane Database of Systematic Reviews. May 16, 2012;(5):CD001141. DOI: 10.1002/14651858.CD001141.pub4
- [78] World Health Organization. WHO Global Data Bank on Infant and Young Child Feeding (IYCF) [Internet]. 2009. Available from: http://www.who.int/nutrition/data-bases/infantfeeding/countries/en/ [Accessed: Februray 19, 2015]
- [79] Aditi A, Graham DY. Vitamin C, gastritis, and gastric disease: A historical review and update. Digestive Diseases and Sciences. 2012;57(10):2504-2515. DOI: 10.1007/s10620-012-2203-7
- [80] Olivares M, Pizarro F, Hertrampf E, Fuenmayor G, Estevez E. Iron absorption from wheat flour: Effects of lemonade and chamomile infusion. Nutrition. 2007;23:296-300
- [81] Cook JD, Reddy MB. Effect of ascorbic acid intake on nonheme-iron absorption from a complete diet. The American Journal of Clinical Nutrition. 2001;73:93-98
- [82] Banjari I. Ditch and Switch: How much supplements do we actually need? Medicinski Pregled. 2014;67(7-8):261-263
- [83] West Jr KP, Shamim AA, Mehra S, Labrique AB, Ali H, Shaikh S et al. Effect of maternal multiple micronutrient vs iron-folic acid supplementation on infant mortality and adverse birth outcomes in rural Bangladesh. The JiVitA-3 randomised trial. Journal of the American Medical Association. 2014;312(24):2649-2658
- [84] Christian P, Shrestha J, LeClerq SC, Khatry SK, Jiang T, Wagner T et al. Supplementation with micronutrients in addition to iron and folic acid does not further improve the hematologic status of pregnant women in rural Nepal. Journal of Nutrition. 2003;133:3492-3498
- [85] Petry N, Olofin I, Boy E, Donahue Angel M, Rohner F. The effect of low dose iron and zinc intake on child micronutrient status and development during the first 1000 days of life: A systematic review and meta-analysis. Nutrients. 2016;8:773

- [86] Rasmussen S, Bergsjø P, Jacobsen G, Haram K, Bakketeig LS. Haemoglobin and serum ferritin in pregnancy—Correlation with smoking and body mass index. European Journal of Obstetrics Gynecology and Reproductive Biology. 2005;123:27-34
- [87] Kallen K. The impact of maternal smoking during pregnancy on delivery outcome. European Journal of Public Health. 2001;11(3):329-333
- [88] Drewnowski A. The cost of US foods as related to their nutritive value. The American Journal of Clinical Nutrition. 2010;92:1181-1188
- [89] Drewnowski A. The Nutrient Rich Foods Index helps to identify healthy, affordable foods. The American Journal of Clinical Nutrition. 2010;91(Suppl):1095S-1101S
- [90] Bucholz EM, Desai MM, Rosenthal MS. Dietary intake in head start vs non-head start preschool-aged children: Results from the 1999-2004 National Health and Nutrition Examination Survey. Journal of the American Dietetic Association. 2011;111(7):1021-1030
- [91] Drewnowski A. Obesity and the food environment: Dietary energy density and diet costs. American Journal of Preventive Medicine. 2004;27(3S):154-162
- [92] Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: A systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014;384:766-781
- [93] Raatikainen K, Heiskanen N, Heinonen S. Transition from overweight to obesity worsens pregnancy outcome in a BMI-dependent manner. Obesity. 2006;**14**(1):165-171
- [94] DeVader SR, Neeley HL, Myles TD, Leet TL. Evaluation of gestational weight gain guidelines for women with normal prepregnancy body mass index. Obstetrics & Gynecology. 2007;110:745-751
- [95] Morken N-H, Klungsøyr K, Magnus P, Skjærven R. Pre-pregnant body mass index, gestational weight gain and the risk of operative delivery. Acta Obstetricia et Gynecologica Scandinavica. 2013;92:809-815
- [96] Hutcheon JA, Lisonkova S, Joseph KS. Epidemiology of pre-eclampsia and the other hypertensive disorders of pregnancy. Best Practice & Research Clinical Obstetrics & Gynaecology. 2011;25:391-403
- [97] Flick AA, Brookfield KF, de la Torre L, Tudela CM, Duthely L, González-Quintero VH. Excessive weight gain among obese women and pregnancy outcomes. American Journal of Perinatology. 2010;27(4):333-338
- [98] Godfrey KM, Reynolds RM, Prescott SL, Nyirenda M, Jaddoe VW, Eriksson JG, Broekman BF. Influence of maternal obesity on the longterm health of offspring. Lancet Diabetes Endocrinol. 2017;5(1):53-64. DOI: 10.1016/S22138587(16)301073
- [99] Gillman MW, Ludwig DS. How early should obesity prevention start? The New England Journal of Medicine. 2013;**369**(23):2173-2175
- [100] Choi S-K, Park I-Y, Shin J-C. The effects of pre-pregnancy body mass index and gestational weight gain on perinatal outcomes in Korean women: A retrospective cohort study. Reproductive Biology and Endocrinology. 2011;9:6. DOI: 10.1186/1477-7827-9-6

- [101] Trandafir LM, Temneanu OR. Pre and post-natal risk and determination of factors for child obesity. Journal of Medicine and Life. 2016;9(4):386-391
- [102] Eriksson JG, Sandboge S, Salonen MK, Kajantie E, Osmond C. Longterm consequences of maternal overweight in pregnancy on offspring later health: Findings from the Helsinki Birth Cohort Study. Annals of Medicine. 2014;46(6):434-438. DOI: 10.3109/07853890.2014.919728
- [103] Lobstein T, Jackson-Leach R. Planning for the worst: Estimates of obesity and comorbidities in school-age children in 2025. Pediatric Obesity. 2016;11:321-325
- [104] Hanson M, Barker M, Dodd JM, Kumanyika S, Norris S, Steegers E et al. Interventions to prevent maternal obesity before conception, during pregnancy, and post partum. Lancet Diabetes Endocrinol. 2017;5(1):65-76. DOI: 10.1016/S2213-8587(16)30108-5
- [105] Grow HMG, Cook AJ, Arterburn DE, Saelens BE, Drewnowski A, Lozano P. Child obesity associated with social disadvantage of children's neighborhoods. Social Science & Medicine. 2010;71(3):584-591
- [106] Monsivais P, Aggarwal A, Drewnowski A. Are socioeconomic disparities in diet quality explained by diet cost? Journal of Epidemiology and Community Health. 2012;66(6):530-535