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ACTA REVIEW

Iron status and iron balance during pregnancy. A critical reappraisal of iron supplementation

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Background. Iron supplementation in pregnancy is a controversial issue. The aim of this review was to summarize the results of relevant papers on this subject.
Methods. Placebo-controlled studies on iron treatment in pregnancy were identified from the Cochrane database.
Results. Among fertile women, 20% have iron reserves of >500 mg, which is the required minimum during pregnancy; 40% have iron stores of 100–500 mg, and 40% have virtually no iron stores. The demand for absorbed iron increases from 0.8 mg/day in early pregnancy to 7.5 mg/day in late pregnancy. Dietary iron intake in fertile women is median 9 mg/day, i.e. the majority of women have an intake below the estimated allowance of 12–18 mg/day. Iron absorption increases in pregnancy, but not enough to prevent iron deficiency anemia in 20% of women not taking supplementary iron. Iron-treated pregnant women have greater iron reserves, higher hemoglobin levels, and a lower prevalence of iron deficiency anemia than placebo-treated women both in pregnancy as well as postpartum. Furthermore, children born to iron-treated mothers have higher serum ferritin levels than those born to placebo-treated mothers. An iron supplement of 65 mg/day from 20 weeks of gestation is adequate to prevent iron deficiency anemia.
Conclusions. In order to avoid iron deficiency in pregnancy, prophylactic iron supplement should be considered. Iron supplements may be administered on a general or selective basis. The selective approach implies screening with serum ferritin in early pregnancy, in order to identify women who can manage without prophylactic iron.

Key words: ferritin; hemoglobin; iron metabolism; iron supplementation; meta analysis; placebo-controlled studies; pregnancy

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The debate concerning prophylactic iron supplements to pregnant women has been controversial, and no definite consensus has been reached on this important matter (1, 2). The Food and Agriculture Organization of The United Nations (FAO) states that: 'Iron requirements in the second and third trimesters cannot be satisfied by dietary iron alone, even if it is of high bioavailability and, unless stores of about 500 mg are believed to exist before pregnancy, administration of iron supplements may be indicated if impairment of the expected increase in hemoglobin mass in the mother is to be avoided' (3). The Department of Health in the United Kingdom states that: 'Ideally all women of childbearing age should have sufficient stores to cope with the metabolic demands made by pregnancy which can be met without further increase because of cessation of menstrual losses and by mobilization of maternal iron stores and increased intestinal absorption. However, when iron stores are inappropriately low at the start of pregnancy,

Abbreviations:
Hb: hemoglobin; SEM: standard error of the mean; SF: serum ferritin; TfR: transferrin receptor; sTfR: soluble transferrin receptor.

supplementation with iron may be necessary' (4). The European Union in its guidelines concludes that: 'The physiologic solution for covering the high iron requirements in pregnancy is to use iron from stores. The problem, however, is that very few women, if any, have iron stores of this magnitude. Therefore, daily iron supplements are recommended in the latter half of pregnancy' (5). The Nutrition Recommendations of the Nordic Countries state that: 'Iron balance during pregnancy requires iron stores of approximately 500 mg. The physiologic need for iron during the later part of pregnancy cannot be supplied solely through the diet' (6).

How much iron do pregnant women require?

In pregnancy, the estimated daily demand for absorbed iron increases gradually from 0.8 mg in the first 10 weeks, to 3.7 mg at 11–20 weeks, 5.7 mg at 21–30 weeks, and 7.5 mg at 31–40 weeks of gestation. The average daily demand for iron in pregnancy is approximately 4.4 mg (7–9).

The major fraction of absorbed iron is used to increase the woman's erythrocyte mass, to fulfil the iron demands of the fetus and to cover blood losses at delivery. The iron content of the newborn baby is dependent on the birth weight, being approximately 200 mg at a weight of 2500 g, and 270 mg at a weight of 3500 g (10). Pregnancies resulting in large babies therefore put greater demands on the future mother's iron reserves than pregnancies resulting in small babies.

The total demand for iron during a single pregnancy is approximately 1240 mg (Table I). From this figure should be deducted the amount of iron being returned to the storage compartment, when the mother's erythrocyte mass after delivery becomes reduced to prepregnant levels. Furthermore, the pregnant woman 'saves' on the average 130 mg iron due to pregnancy-induced amenorrhea.

Table I. Estimated iron requirements in normal pregnancy and delivery

	Amount of iron
Gross iron losses	
Obligate iron loss (0.8 mg×290 days)	230 mg
Expansion of erythrocyte mass	450 mg
Newborn (birth weight 3500 g)	270 mg
Placenta and umbilical cord	90 mg
Blood loss at delivery	200 mg
Total	1240 mg
Net iron losses	
Postpartum decline in erythrocyte mass	+450 mg
Total	**790 mg**

Therefore, the net iron loss strictly associated with pregnancy is approximately 430 mg (newborn 270 mg + placenta 90 mg + blood loss at delivery 200 mg=560 mg−amenorrhea 130 mg=430 mg) (8, 9).

Iron absorption during pregnancy

Studies on intestinal iron absorption in pregnancy have been performed using radioactive ^{59}Fe and whole body counting (7, 11), as well as stable iron isotopes (12). The absorption displays great variation between studies, due to different methods and sizes of the carrier doses, which impede a direct comparison of the results. All studies, however, demonstrate increasing absorption with gestational age. The increase in absorption is most pronounced after 20 weeks of gestation and peaks in late pregnancy. Svanberg (7), using a carrier dose of 100 mg Fe^{2+}, recorded mean absorption values of 7, 9, and 14% at 12, 24 and 36 weeks of gestation, respectively. Heinrich et al. (11) chose a carrier dose of 0.56 mg Fe^{2+} and found mean absorption values of 50, 80 and 90% at 16–20, 24–28 and 32–36 weeks of gestation, respectively. Barrett et al. (12) used stable iron isotopes and a total oral iron dose of 6 mg Fe^{2+}, consumed in an English breakfast meal. The mean iron absorption was 7,36 and 66%, at 12, 24 and 36 weeks of gestation, respectively, with great individual variations. Twenty weeks postpartum absorption declined to 11%.

Dietary iron intake in pregnancy

The median dietary iron intake in fertile, non-pregnant Danish women is 8.5–9.1 mg/day (13), i.e. in the majority intake is below the estimated dietary allowance of 12–18 mg/day (6).

The energy intake and the composition of the diet in pregnancy was similar to prepregnancy levels in a Norwegian survey on 821 women, examined at 17 and 33 weeks of gestation (14). The mean energy intake was 8.9 MJ/day at both examinations (14), which is identical to the energy intake in non-pregnant Danish women (13). At both examinations, the mean dietary energy distribution of protein, fat, and carbohydrate was 14, 36 and 50% (14). Women who smoked had lower intake of protein, vitamin C, and iron compared with non-smokers. The mean dietary iron intake was 11 mg/day both in early as well as in late pregnancy, and 96% of the women had an intake below 18 mg/day (14).

The iron balance is influenced by the amount of iron contained in the diet, and by the bioavailability of the consumed iron. Dietary iron intake is proportional to the energy intake. Nearly all

Western European women have a dietary iron intake, which is inadequate to fulfil the demands in middle and late pregnancy (3–6). The low dietary iron intake is primarily due to a low energy intake, which is a consequence of the sedentary lifestyle prevailing in the Western societies.

Dietary iron absorption can be increased by consumption of food with a high content of iron with a high bioavailability, first of all beef, pork, poultry, fish and food products containing oxblood or pig's blood with hem iron (15). Hem iron is more readily absorbed than non-hem iron (16). Furthermore, meat contains factors which enhance the absorption of non-hem iron (16). Calf's liver and pig's liver has a high iron content, but should be consumed in moderate quantities in pregnancy due to the high content of vitamin A, which may exert teratogenic effects. Iron absorption is impaired by calcium phosphate in milk and cheese, by polyphenols in coffee and tea and by foods containing phytate (16). Even under ideal conditions, at the most 30% of the food iron content can be absorbed, corresponding to 3 mg iron/day at a food iron intake of 9 mg/day, i.e. significantly less than the daily requirements in pregnancy. A higher food iron intake with a higher bioavailability implies fundamental changes in the nutritional habits, and it is not realistic to assume that such changes can be implemented in pregnant women. Since dietary iron cannot cover iron requirements in the majority of pregnant women, recent guidelines now refrain from giving specific figures for recommended dietary iron intake (3–6).

Iron status in fertile, non-pregnant women

Mobilizable body iron stores, i.e. the iron which is available for synthesis of hemoglobin and iron containing enzymes, can be estimated by measurement of the serum ferritin concentration (17, 18). In healthy, non-pregnant women, and in women with simple iron deficiency and iron overload, each μg/L of serum ferritin corresponds to 7–8 mg of mobilizable iron (17). Serum ferritin values of <15 μg/L indicate absent iron stores, i.e. iron deficiency (19, 20). Serum ferritin values in the range of 15–30 μg/L indicate small iron stores, i.e. no stainable hemosiderin iron in the bone marrow, whereas ferritin values of >30 μg/L are indicative of the presence of stainable bone marrow iron (19).

How is iron status in fertile non-pregnant women? A survey in 1988 of women aged 35–45 years, demonstrated a median serum ferritin of 40 μg/L (21). Thirty-three percent had small or absent iron stores (serum ferritin ≤ 30 μg/L), and 22% had serum ferritin values of >70 μg/L. Another survey in 1992 of women aged 18–30 years, also showed a median serum ferritin of 39 μg/L (22). Forty-one percent had small or absent iron stores (serum ferritin ≤ 30 μg/L) and 14% had serum ferritin values of >70 μg/L. These surveys demonstrate that fertile women have estimated median body iron stores of 300 mg. Between 33–41% have no bone marrow hemosiderin iron, and start pregnancy with an unfavorable iron balance. Only 14–22% have iron stores of more than 500 mg, which balance the net iron loss in pregnancy (8, 9).

Iron status in pregnancy

In pregnancy, characteristic changes are observed in hemoglobin and serum ferritin. The physiologic increase in plasma volume of approximately 50% is only partially compensated by a concomitant increase in the erythrocyte mass of approximately 25%. The subsequent decline in the hemoglobin concentration, i.e. the hemodilution of pregnancy, reaches its maximum at 24–32 weeks of gestation and subsequently decreases in late pregnancy (Fig. 1) (23, 24). The degree of hemodilution displays great individual variation, i.e. women with similar total erythrocyte masses may have different hemoglobin concentrations, which can vary with at least 30 g/L. Hemoglobin is therefore not suitable as a single parameter to estimate body iron stores or iron status during pregnancy.

Serum ferritin levels display a gradual fall with nadir at 35–38 weeks of gestation, followed by a slight increase in late pregnancy (Fig. 1) (25). In spite of these physiologic fluctuations, the association between serum ferritin and iron stores estimated by bone marrow hemosiderin iron also exists in pregnancy, and serum ferritin is the most reliable marker of gestational iron status we have at the present (26, 27). Due to the physiologic decline (25), a critical serum ferritin value of <12 μg/L should be employed as indicator for gestational iron deficiency. The ideal definition of iron deficiency anemia states that treatment with iron should induce a significant increase in hemoglobin. This criterion cannot be fulfilled in the clinical situation. Instead, an arbitrarily chosen hemoglobin level is employed as discriminatory value in the definition of anemia. The World Health Organization has suggested that a critical value of 110 g/L (6.8 mmol/L) should be used in pregnancy (28). A recently published study shows that a critical value of 105 g/L (6.5 mmol/L) is more appropriate (24). Table II shows the prevalence of iron deficiency in placebo-treated and iron-treated pregnant women. In late pregnancy, 50% of placebo-treated women display serum ferritin values of <12 μg/L; 21% have serum ferritin values of <12

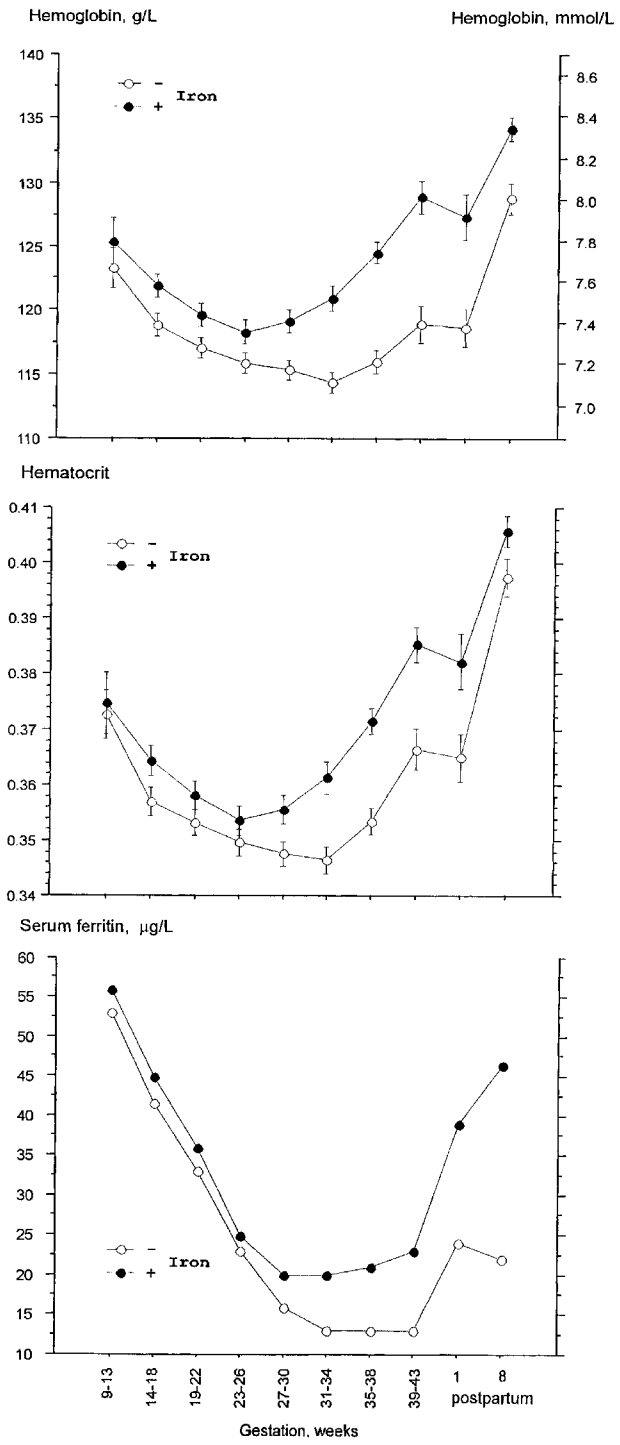

Fig. 1. Variations in hemoglobin and hematocrit (mean±SEM) as well as serum ferritin (median) in normal pregnancy and postpartum in placebo-treated and iron-treated women taking 66 mg ferrous iron daily. Based on ref. 24 and 25.

µg/L and hemoglobin values compatible with iron deficiency anemia.

The transferrin receptor (TfR) is primarily expressed on the surface of erythroid cells, and the density of TfR increases in iron deficiency (29). Shed TfR circulates in the blood as soluble TfR (sTfR). The serum sTfR is assumed to be proportional to the density of TfR on erythroid cells, i.e. in iron deficiency serum sTfR increases (29). Serum sTfR renders information about cellular iron deficiency, in contrast to serum ferritin which gives information about iron reserves. When iron reserves are exhausted, serum sTfR increases (29). Serum sTfR appears to be a useful indicator, capable of identifying women with low serum ferritin, who have more significant iron deficiency (30, 31). The mean serum sTfR concentration in iron replete pregnant women does not differ from the concentration in non-pregnant women (30). In women with depleted iron stores, serum sTfR levels of >8.5 mg/L indicate iron deficiency (30). Serum sTfR seems to be a sensitive marker of iron deficiency in pregnancy, and by combining serum sTfR and serum ferritin measurements, the entire spectrum of iron status in pregnancy can be assessed (30, 31).

The serum erythropoietin level increases gradually in pregnancy and peaks at the end of the 3rd trimester (32). The increase is significantly higher in placebo-treated women compared with iron-treated women (32). This difference in the erythropoietin response signals that the lower hemoglobin levels in placebo-treated women, which are due to iron deficiency anemia, by the body is recognized as being abnormal and triggers off a physiologic erythropoietin response, in order to further stimulate erythropoiesis.

Iron supplementation in pregnancy, placebo-controlled studies

The Cochrane database was searched for controlled studies on iron supplementation in gestation. All studies on iron treatment in pregnancy have unequivocally shown that placebo-treated women have significantly lower serum ferritin and hemoglobin than iron-treated women (Table III) (7, 24, 25, 33–39). This difference persists until at least 24 weeks postpartum (7, 24, 25, 33, 34, 36, 39). The studies also demonstrate that many women not using iron supplements have iron deficiency and iron deficiency anemia.

High doses of supplementary iron, 100–200 mg daily, have been recommended to pregnant women (7, 34, 35, 37, 40, 41). A daily dose of 200 mg iron has a significant impact on hematologic indices, and increases both serum ferritin and hemoglobin at term to levels observed in non-pregnant women (40, 41). Sjöstedt et al. (40) found that the maximum increase in hemoglobin was obtained with a daily dose of 100 mg iron. Accordingly, a multivitamin-mineral tablet designed for pregnant women

Table II. Prevalence of iron deficiency, low hemoglobin and iron deficiency anemia in normal pregnancy and postpartum. Treatment with 66 mg ferrous iron daily was given from 18 weeks of gestation. Based on ref. 24 and 25

	Gestation (weeks)							Postpartum (weeks)
	14–18	19–22	23–26	27–30	31–34	35–38	39–43	8
n	46	57	56	56	57	57	24	58
Placebo								
Iron deficiency (% of women)*	4.4	5.3	19.6	32.1	47.4	49.1	50.0	15.5
Low hemoglobin (%)**	19.6	14.0	5.4	16.1	19.3	29.8	41.7	25.7
Iron deficiency anemia (%)***	0	0	0	5.4	10.5	17.5	20.8	12.1
n	47	61	62	61	62	59	29	62
Iron								
Iron deficiency (% of women)*	2.1	1.6	3.2	9.8	8.1	5.1	3.5	3.2
Low hemoglobin (%)**	8.5	4.9	1.6	3.3	4.8	8.5	10.3	6.5
Iron deficiency anemia (%)***	0	0	0	0	0	0	0	1.6
Low hemoglobin (5th %-tile, g/L)	109	106	103	105	105	110	115	123
p-value*	NS	NS	0.01	0.006	<0.0001	<0.0001	<0.0003	0.04
p-value**	NS	NS	NS	0.04	0.03	0.007	0.02	0.008
p-value***	NS	NS	NS	NS	0.03	0.002	0.03	0.05

p-values (χ^2-test with Yates's correction) indicate significance of differences between placebo-treated and iron-treated women.
Iron deficiency: serum ferritin <12 μg/L in pregnancy and <15 μg/L postpartum.
Low hemoglobin: <5th percentile in iron-treated women according to stage of pregnancy and postpartum (ref. 24). Hb in g/L×0.062054=Hb in mmol/L.
Iron deficiency anemia: serum ferritin <12 μg/L in pregnancy and <15 μg/L postpartum and hemoglobin <5th percentile according to stage of pregnancy and postpartum.

(Duo-Feron® Vitamin, Astra) contains 100 mg ferrous iron.

Iron supplements in pregnancy should be adequate to prevent iron deficiency anemia in all women. Because of the possible negative interaction of iron on the intestinal absorption of other essential divalent cations (zinc, copper, chromium, molybdenum, manganese, magnesium, calcium) (16, 42–45) the iron dose should be as low as possible in order to fulfil its purpose. In a placebo-controlled study, half of the pregnant women were randomized to daily treatment with placebo tablets and the other half to treatment with 66 mg ferrous iron from 20 weeks of gestation (24, 25). Fifty percent of the placebo-treated women developed iron deficiency (serum ferritin <12 μg/L) and 21% displayed iron deficiency anemia in the 3rd trimester. Among the iron-treated women, 10% presented with iron deficiency in late pregnancy, but none had iron deficiency anemia (Table II).

Both Taylor et al. (36) and Milman et al. (25) have demonstrated that a daily supplement of 65 mg ferrous iron in pregnancy is adequate to prevent iron deficiency in 80–90% of the women and to prevent iron deficiency anemia in all women. Galan et al. (38) reported a similar effect of 40 mg ferrous iron daily. Even a daily dose of 27 mg iron has a recognizable positive effect on iron status (39). The minimum effective dose of iron which prevents iron deficiency anemia is not clarified. However, a daily dose of 18 mg iron taken as a multivitamin-mineral tablet is inadequate to prevent iron deficiency (46).

Iron supplements should be administered from early pregnancy. However, as iron absorption increases with gestational age, it is proper to start iron treatment at the latest from 20 weeks of gestation. Iron tablets should be taken between meals in order to ensure optimum absorption. Gastrointestinal side effects are non-existent at iron doses below 70 mg/day and cannot be used as an argument against prophylactic iron treatment.

Iron status after delivery

Immediately after delivery, serum ferritin and hemoglobin are influenced by the acute blood losses. Later postpartum, when the circulation has become stabilized, there is an increase in both serum ferritin as well as hemoglobin, which is most pronounced in iron-treated women (Fig. 1). Eight weeks after an uncomplicated delivery, 61% of placebo-treated mothers had small iron stores (serum ferritin 15–30 μg/L), 16% had iron deficiency and 12% had iron deficiency anemia. Among iron-treated women, 3% had iron deficiency and 1.6% had iron deficiency anemia (Table II).

In the postpartum period, iron deficiency anemia is inexpedient considering the physical and mental demands of the newborn baby. In 5–10% of deliveries, peripartum bleeding causes a significant postpartum anemia (25, 47, 48). The limiting fac-

Table III. Placebo-controlled studies on iron treatment in pregnancy. The table shows the lowest recorded, corresponding values of hemoglobin and/or serum ferritin

	Treatment	Women (*n*)	Ferrous iron (mg/day)	Study period	Results – lowest recorded values in study period
Fleming et al. 1974 (33)	placebo	21		20 weeks	48% Hb <100 g/L
	iron	17	60	to term	12% Hb <100 g/L
Svanberg 1975 (7)	placebo	26		12 weeks	Hb mean 114 g/L
	iron	24	200	to term	Hb mean 120 g/L
Puolakka et al. 1980 (34)	placebo	16		16 weeks	SF median 21 μg/L; Hb mean 109 g/L (38% <110 g/L)
	iron	16	200	to term	SF median 63 μg/L; Hb mean 115 g/L (0% <110 g/L)
Foulkes & Goldie 1982 (35)	placebo	250		12 weeks	Low SF; 18% Hb <105 g/L
	iron	251	100	to term	Higher SF; 5% Hb <105 g/L
Taylor et al. 1982 (36)	placebo	24		12 weeks	SF median 5 μg/L; Hb mean 111 g/L
	iron	21	65	to term	SF median 15 μg/L; Hb mean 119 g/L
Romslo et al. 1983 (37)	placebo	23		12 weeks	SF mean 5 μg/L (83% <10 μg/L) 30% Hb <110g/L
	iron	22	200	to term	SF mean 15 μg/L (5% <10 μg/L) 9% Hb <110 g/L
Galan et al. 1990 (38)	placebo	84		12 weeks	SF median 10 μg/L (65%<13 μg/L) Hb mean 117 g/L 26% Hb <110 g/L
	iron	81	40	to term	SF median 19 μg/L (30% <13 μg/L) Hb mean 121 g/L 4% Hb <110 g/L
Milman et al. 1991 (25)	placebo	57		14 weeks	SF median 12 μg/L (28% <10 μg/L) Hb mean 114 g/L (25% <110 g/L) 12% iron deficiency anemia (SF <12 μg/L and Hb <110 g/L)
	iron	63	66	to term	SF median 21 μg/L (3% <10 μg/L) Hb mean 119 g/L (12% <110 g/L) 0% iron deficiency anemia
Eskeland et al. 1997 (39)	placebo	23	27	20 weeks	17% iron deficiency anemia (SF <15 μg/L and Hb <100 g/L)
	iron	48		to term	0% iron deficiency anemia
Milman et al. 1999 (24)	placebo	108		9 weeks	Hb mean 114 g/L (34% <110 g/L)
	iron	99	66	to term	Hb mean 118 g/L (17% <110 g/L)

Hb=hemoglobin; SF=serum ferritin.

tor for correction of anemia is the lack of body iron reserves at the end of pregnancy (25, 47, 48). In order to avoid blood transfusions, some obstetricians have suggested treatment with recombinant erythropoietin and intravenous iron (47, 48). It would seem more physiologic if the mother's iron reserves were adequate to compensate for blood losses at delivery. Therefore, women taking iron supplements in pregnancy should continue iron treatment at least until 8 weeks postpartum.

One single pregnancy puts a fingerprint on iron status for many years. Nullipara have higher serum ferritin than unipara, who in turn have higher ferritin than multipara (49). These differences can be recognized even after the menopause.

Iron status in newborn babies

Iron is transported across the placental membrane by an active process, which is mediated via binding of maternal transferrin bound iron to transferrin receptors in placenta and subsequent transfer of iron into the fetal circulation (50–52). The efficiency of this transport system implies that iron deficiency in the newborn is encountered only at extreme iron deficiency in the mother. Iron deficiency in mature newborn babies is a rare event in the Western Countries.

The newborn's iron status may depend on the pregnant woman's iron status. At delivery, there is a correlation between the mother's and the newborn's serum ferritin (41). Children born to iron-treated mothers have higher serum ferritin than children born to placebo-treated mothers (25, 37, 53). The higher ferritin levels in newborns of iron-treated women suggest that these babies have a higher iron content and therefore a lower risk of contracting iron deficiency within the first years of life (53, 54). Another important determinant of the newborn's iron status is the amount of blood transfused from the placenta before the clamping of the umbilical cord (55).

Pregnant women's hemoglobin and newborn's birth weight are inversely correlated already from the beginning of the second trimester, before the maximum decline in hemoglobin has occurred (56–58). A low hemoglobin is associated with a low blood viscosity, which increases placental perfusion, and is assumed to result in a better nutrition of the fetus (57). From this point of view, optimum hemoglobin levels in the second trimester range between 96–115 g/L (6.0–7.1 mmol/L) (57). Birth weight decreases both at low hemoglobin levels of <86 g/L (5.3 mmol/L), and at high levels of >145 g/L (9.0 mmol/L) (57). The association between a high hemoglobin in pregnant women

and a low birth weight of the newborn is first of all due to inadequate hemodilution in a fraction of the women. It predisposes to preeclampsia and eclampsia, both of which are associated with a low birth weight of the newborn (58).

Pro et contra iron supplementation

The attitude pro et con routine iron supplementation in pregnancy has been overwhelmed more by teleologic than by rational arguments. The first main issue is whether or not routine iron treatment has a detrimental effect on the outcome of pregnancy. Due to the inverse correlation between the future mother's hemoglobin and the newborn's birth weight, some obstetricians consider gestational iron deficiency to be a normal physiologic phenomenon, and therefore oppose iron prophylaxis (59–61). If this argument was to be correct, iron treatment should increase the frequency of perinatal complications and the prevalence of low birth weight in the newborn. However, placebo-controlled studies have shown no harmful effect of iron supplementation (7, 25, 34–38, 53). A placebo-controlled study from a developing country demonstrated that iron treatment induced a marked decrease in the prevalence of gestational and postpartum iron deficiency anemia (53). In addition, serum ferritin, body length and apgar score were higher in infants of women in the iron-treated group (53). A large Nordic survey on pregnant women, randomized to either routine treatment with 100 mg ferrous iron daily, or to selective treatment with the same dose if the hematocrit dropped below 0.31, did not find any detrimental effect of iron treatment (62). On the contrary, there was a higher frequency of gestational complications, and lower birth weights of the newborns in selectively iron-treated women compared with routinely treated women. Postpartum, routinely iron-treated women had significantly higher hematocrit than selectively treated women (62).

Among those who consider iron treatment not to be harmful, the second main issue is whether or not is has any beneficial effect (2). If the effect parameters are chosen as 'hard' end-points, such as the newborn's birth weight or perinatal morbidity or mortality in mother and child (2), there is most likely a marginal or no effect of routine iron supplementation in women in affluent societies. When the effect parameters, however, are chosen as 'soft' end-points, such as:

1. higher hemoglobin levels and absence of iron deficiency anemia, thereby increasing physical fitness and well-being in the pregnant women;
2. greater iron reserves in the mother in order to prevent postpartum iron deficiency anemia due to blood losses at delivery;
3. greater iron reserves in the newborn in order to prevent iron deficiency in the first years of life, then routine iron supplementation could be of benefit.

General or selective iron prophylaxis?

General iron prophylaxis means treatment of all pregnant women, whereas selective prophylaxis implies treatment of women who are at risk for iron deficiency. From a nutritional point of view, selective iron prophylaxis should be preferred. Women at risk for iron deficiency can be identified by measurement of serum ferritin. Using this approach, women with adequate iron stores will avoid unnecessary treatment with iron which could be potentially harmful in those 12–13% of women being heterozygous and those 0.3–0.5% being homozygous for the *HFE*-gene coding for hereditary hemochromatosis (63). Serum ferritin should be analyzed either prior to pregnancy, or in early pregnancy. Such a strategy is recommended in Norway (64, 65). The Swedish guidelines advocate routine iron supplementation with 100 mg iron daily from 20 weeks of gestation (The Swedish National Board of Nutrition, personal communication), and The Danish National Board of Health recommends prophylactic iron, 60–70 mg daily, to all pregnant women from 20 weeks of gestation (66).

Iron status markers in early gestation display no clinically significant correlations with values in late pregnancy and postpartum and cannot be used as guidelines for iron prophylaxis with individually tailored iron doses (67). When iron status 8 weeks postpartum is chosen as endpoint, then serum ferritin can be employed to identify women who can manage without iron prophylaxis (68). Women having prepregnancy serum ferritin values of >80 μg/L, or values of >70 μg/L in early gestation, can complete pregnancy without postpartum iron deficiency. The sensitivity of this discriminatory ferritin value is 100% (68). In early pregnancy, 20% of women have serum ferritin values of >70 μg/L (25). It would be convenient if the Nordic Countries could reach consensus on Maternity Welfare concerning common guidelines on the monitoring of iron status and iron supplementation in pregnancy.

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