Original scientific paper
616.155.194.8:618.8

IRON DEFICIENCY ANAEMIA IN PREGNANCY

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Abstract

Anaemia due to iron (Fe^{++}) deficiency or sideropenic anaemia is manifested when due to the lack of iron (Fe^{++}) sufficient haemoglobin (Hb) cannot form which is essential for erythrocyte (Er) oxygenation. Angiopenic anaemia is a common occurrence during pregnancy and it is a concern for the mother because it is related to the birth of the baby with lower body weight, premature birth and mortality of pregnant women. Symptoms are: fatigue, inaptability, malaise, lack of concentration, insomnia, palpitations, paleness of mucous membranes and the skin, light breathing etc. In the United States and Europe (15-25% of staff), iron deficiency is the main cause of anaemia during pregnancy.
Materials and Methods: The study included 300 pregnant women with an average age of 25.00 ±9.50 years. For the examination, we used the Concentrations of Erythrocytes, Haemoglobin (Hb), Haematocrit (Htc) and Iron, with measurements ranging from the first, second and third quarters. **Results:** From the obtained results for the examined parameters by the brutal gratitude in the third trimester a significant difference (for Er, Hb, Htc, Fe^{++}) was observed for $p < 0.0001$ in the first and second quarters compared to the third trimester and the healthy control group, compared with the healthy female control group (No-250). **Conclusion**: Prevention of anaemia during pregnancy should be corrected primarily by food as well as, in the most severe cases, with iron supplements (from 30-60 mg Fe^{++} every day), folic acid and vitamin B12. The follow-up of pregnancy anaemia and supplementation with Fe^{++} should be the first step of primary doctors and gynaecologists to initiate initial pregnancy anaemia symptoms in order to prevent and mitigate its effects on mother and foetus.

Keywords: iron deficiency, anaemia pregnancy.

INTRODUCTION

Pregnancy anaemiais a significant risk factor contributing to the foetus and mother morbidity, and it is considered a global health problem, with a prevalence of approximately 50-80% of the pregnant women. Iron-deficiency anaemia can lead to premature birth, with a low-body-mass of the baby, memory deficiency, hearing deficiency, which reflect with lack of memory, inability to learn, and all of these characteristics manifest in the adult life also (HOI 2001,WHO 2011). Iron-deficiency is the most common cause of pregnancy anaemia, which has always been associated with lack of folate andvitamin B12 (cyanocobalamin). During pregnancy, it is of uttermost importance detection of iron deficiency and prevention of complications arising from the iron deficiency in the pregnant mother's organism.According to the World Health Organization (WHO), pregnancy anaemia is considered when the parameters' values are Hb<11 g/dL or Htc<33% during the first and third trimesters and Hb <7 g/dL, <10.5 g/dL or Htc< 32% during the second trimester, while very severe anaemia is considered when the values of the parameters are Hb <4 g/dL (HOI 2001,WHO 2011). Globally, the most common cause of pregnancy anaemia is iron-deficiency resulting from transferrin deficiency, which in turn is the result of low reserves of iron.A study of the Nutrition Impact Model, a systematic analysis from 257 sources of population data from 107 countries, estimated that the global prevalence of pregnancy anaemia is 33-43% (in the 2011)(Stevens GA *et al.*, 2013). Maternal

risks include fatigue, pallor, tachycardia, poor physical activity tolerance, a need for blood transfusion, causing preeclampsia or placental abruption, cardiac failure, and unexpected death. In a common pregnancy, the mother's requirements for iron include 300-350 mg for the foetus and placenta, 500 mg to increase the total erythrocyte mass, and 250 mg to compensate the loss of blood during labour and delivery. Iron requirements gradually increase from 0.8 mg per day in the first trimester to 7.5 mg per day in the third trimester However, daily average iron absorption with the Western diets is only 1-5 mg. Therefore, women cannot meet their iron needs with normal food consumption, thus it is preferable to consume iron-rich preparations to supplement the iron reserve depots in order to prevent the anaemia and its consequences. WHO recommends that all pregnant female consume a 30-60 mg daily dose of iron (De Sá SA *et al.,* 2015). It is estimated that iron deficiency affects approximately 1-2 billion pregnant women, postpartum women, infants, and young children, respectively approximately 50% of pregnant women worldwide are anaemic. Pregnancy anaemia is not only a problem in low- and middle-income countries it is also common in high-income countries (Geng F *et al.,* 2015). The incidence of pregnancy anaemia is 12-18% of pregnant women (women having anaemia signs at birth) in developed countries and 43-75% in underdeveloped countries. Also, the anaemia prevalence, based on different scholars varies, because its appearance also depends on: the place of living, eating habits, social and living conditions, education level, and other specific pathologies in a particular population. Fetal growth and development consist in a high sensitivity for mother's food insufficiency during early pregnancy (Scholl *et al.,* 2011). Iron deficiency is accompanied with extremely low levels of ferritin which progressively decreases during pregnancy, and reaches a low state during 35 – 38 gestational week, and it increases during the month before delivery. Ferritin is a more sensitive and specific marker for iron deficiency, than serum-iron itself, and it is a better estimation for iron-deficiency during pregnancy (Bothwell 2000). Mean Corpuscular Volume (MCV) is an unreliable indicator of iron deficiency during pregnancy. Erythropoiesis stimulation leads to a physiological increase of MCV during pregnancy (Romslo *et al.,* 1983). The recommendations for oral iron-preparation dosage vary 60-200 mg of elemental iron per day. Anaemia due to iron-deficiency or sideropenicanaemia is the form of anaemia during which due to iron-deficiency, the necessary quantity of Hb for oxygenation of body cells by Er, cannot be formed. Lack of iron is the most common cause of anaemia in pregnancy (Camaschella 2015).Pregnancy anaemia is a common problem in obstetric and perinatal care. The values of Hb <10.5 g/dL, regardless of the pregnancy period, may be considered to be anaemia. The aetiology of pregnancy anaemia is multifactorial: erythrocytes abnormalities (congenital – thalassemia),nutritional deficiencies, various inflammations, iron-deficiency, which is also considered as the major cause of pregnancy anaemiain about 20-80% of cases. Lack of iron is due to the lack of iron deposits, weakened erythropoiesis, and iron-deficiency. Pregnancy anaemia may be exacerbated by various bleedings such as gastrointestinal, gynaecological, peripartal, and/or placental haemorrhages. In addition to symptoms related to general anaemia, specific risks for the mother and the foetus exist during pregnancy, such as intrauterine growth retardation, premature birth, etc. Anaemia during pregnancy is a concern for the mother, because if it is not treated, it manifests itself with low body-mass of the new born, premature birth, and it may lead to mortality of the mother and the infant. The clinical manifestation of pregnancy anaemia is dominated by symptoms of: general weakness, inappetence, fatigue, lack of concentration, palpitations, chest discomfort, paleness the mucosae and the skin, dyspnoea, and forced reduced physical activity. Iron supplementation follow-up through random controlled testing may shed light upon the long-term effects of increased consumption of iron during pregnancy in the following results. DDuring pregnancy anaemia there is no lack of blood volume (the total volume of blood remains the same), but the volume of Er will decrease and the volume of the plasma will be parallelly increased. The appropriate terminology to describe the decrease

of the number of Er(consequently the value of Hb) is "erythropenia" (Moretti *et al.,* 2015). In the USA, pregnancy anaemia is the main reason for anaemia during pregnancy. Approximately 15-25% of the pregnant women, experience a lack of iron which is associated with a decrease of the levels of Hb, which may also be caused by a high mass of plasma volume in relation to the decreased volume of Er.

The practical part of this research is related to the haematological changes that occur during normal pregnancy due to anaemia resulting from the iron-deficiency and complications that can lead to the appearance of health complications in pregnant mothers and foetuses.
Based on the results obtained from this research, we propose prophylactic measures by adequate treatment (by proper nutrition and medicament usage) to prevent the frequent occurrence of this phenomena which is manifested during pregnancy anaemia. This scientific work aimed to describe the manner of anaemia manifestation, the tendency of propagation and its relation to the various metabolic processes, in order to identify and verify the difference between the various haematologic markers during the trimesters of the nine months of pregnancy.

MATERIALS AND METHODS

The study included 300 pregnant women with an average age of 2.,0 ±9.5 years old. As a result, we have examined the concentration of Erythrocytes (Er), Haemoglobin (Hb), Haematocrit (Htc), Iron (Fe), and Calcium (Ca), during the first, second, and third trimester.
Results: from the obtained results for the examined parameters for Er, Hb, Htc, Ca, a significant difference of $p < 0.0001$ existed, in relation to the control group of healthy females (No-250).

Table 1. The groups of examined patients, control group and respective average age

Number of patients	Average age ± DS	Control group	Average age ± DS
F = 300	25.0 ±9.5 years old	250	26,4 ±8.0 years old

Processing and interpretation of results obtained from examined female pregnancy

The statistical analyses were conducted by the software package – SPSS (Statistical Package for the Social Science, v.17). The distributions of the obtained results were tested by using the method of Skewness and Kurtosis. The results for the analysed parameters (number of Er, Hb, Htc, MCV, MCH (Mean Corpuscular Haemoglobin), MCHC (Mean Corpuscular Haemoglobin Concentration), iron concentration in serum, total calcium in serum), were obtained by using the fundamental descriptive statistical methods (average value, standard deviation etc.). The differences between the various trimesters of pregnancy (first, second, and third trimester) were analysed by using the analytical method of measuring variance – ANOVA, whereas the differences between the first and second trimester, and second and third trimesters were analysed by implementation of t-test.

Table 2. The values of the Hemogram (Haemoglobin, Erythrocytes, Haematocrit, Calcium before therapy (first, second and third trimester) and the control group

Number of patients	Hb	Er	Htc	Ca	P
F = 300	5.20 ± 1.04 ↓	3.20 ± 0.90 ↓	0.26 ± 0.80 ↓	1.80 ± 0.70↓	0.0001
C.group = 250	8.10 ± 1.10	4.80 ± 1.05	0.68 ± 0.70	2.20 ± 0.90	0.0001

From the obtained results for the examined parameters (Er, Hb, Htc, Ca) from the pregnant and anaemic females (No-300) in the beginning of the study, in comparison to the control group of the healthy females (volunteers – 250) a difference of statistical significance of $p < 0.0001$ was observed.

Table 3. Hemogram value (Haemoglobin, Erythrocytes, Haematocrit, Calcium), after iron supplementary therapy (30 – 60 mg per day, every day), during the first, second and third trimester

Number of patients	Hb	Er	Htc	Ca	P
F = 300	7.90 ± 0.90	4.50 ± 0.70	0.50 ± 0.80	2.10 ± 0.60	NS
C. Group = 250	8.10 ± 1.10	48.0 ± 1.5	0.68 ± 0.70	2.20 ± 0.90	NS

As it may be observed from the table, after 30 – 60 mg of iron supplemented, every day, a significant statistical difference was not observed between the obtained values from the examined patients – pregnant females, and the control group thus proving the positive effects from the iron-supplementary preparations therapy. In the determination of the haematologic profile of the pregnant females, of a significant importance are the erythrocytes' indexes: MCV, MCH, MCHC, and the average concentration of Hb in the erythrocytes). MCV is an important factor which determines the morphological type of the anaemia. On a blood samples from the three trimesters of the pregnancy small differences in MCV were observed for the second trimester. In 100 examined pregnant females for the first trimester (33,33%), 90 examined for the second trimester (30%), and 100 examined for the third trimester (33,33%), the MCV values were within the referent values. Also, the smallest changes were observed during the third trimester, whereas the largest changes were observed during the second trimester (Table 4).

Table 4. Values of MCV in pregnant females during different periods

Referent values of MCV – fL/erythrocyte = 80.0 – 99.00	First trimester	Second trimester	Third trimester
≤ 80.0	150	70	90
81.0-88.0	100	80	110
≥89.0	50	150	100
Total	300 (100%)	300 (100%)	300 (100%)

Between the various trimesters of the pregnancy significant differences are present for the average values of MCV. The lowest values can be observed in the first and third trimester, whereas the highest values can be observed in the second trimester with a statistically significant difference of 0.0001 (Table 4).

The results obtained from our study show that levels of iron in serum below the lowest limit (less than 7.3 μmol/L) were found in 160 examined pregnant females (53.33%) for the first trimester, in 100 (33.33%) for the second trimester, and 40 (13.33) for the third trimester. Also values within the referent values were observed in 100 examined pregnant females (33.33%) for the first and third trimester, but with a reduction to 80 examined pregnant females (26.67%) in the second trimester (Table 4).

Table 5. Serum-Iron Levels in different periods of pregnancy

Referent values for Fe = 7.30 – 23.00 µmol//L	**First trimester**	**Second trimester**	**Third trimester**
≤ 7.3	160 (53.33%)	90 (30%)	60 (20%)
7.3 – 10.0	100 (33.33%)	80 (26.67%)	100 (33.30%)
≥11.0	40 (13.33%)	130 (43.30%)	140 (46.70%)
Total:	300 (100%)	300 (100%)	300 (100%)

The average values of iron in the first trimester achieved a value of 14.0 µmol/L, in the second 13.3 µmol/L, and in the third it was 12.9 µmol/L. The serum iron level was reduced in a progressive manner until the third trimester with a statistically significant difference of $p < 0.0001$ (Table 5).

The presented results help us conclude that by progression of pregnancy the deposited iron reserves are reduced, leading to hypochromic anaemia. The obtained results from our study show that the levels of iron in serum below the normal limit(<11.0 µmol/L) were found in 33 (22%) of the pregnant females during the first trimester, 56 (37.33%) during the second trimester, and 62 (41.33%) during the third trimester (Table 5).

DISCUSSION

Anaemia as a medical term means lack of erythrocytes in the body. Consequence of anaemia is the reduced ability to transfer oxygen from the lungs, via blood and erythrocytes, to all of the body's tissues and cells. The reduction of the erythrocyte's number may happen due to two reasons: production of insufficient quantity of erythrocytes by the bone marrow, misbalanced destruction and production of erythrocytes (more erythrocytes are destroyed, than they are produced). The lifespan of erythrocytes is up to 4 months, and then they are destroyed in order for new erythrocytes to be produced. If this equilibrium is disrupted, and the erythrocytes are destroyed faster, or in a greater quantity than they are created, the state of anaemia arises. Iron, folic acid, and vitamin B12 (cyanocobalamin) are needed for formation of erythrocytes. If a single "building material" is missing (most often iron is the missing material), anaemia arises. During pregnancy the requirement for iron rises two-fold, and by progression of pregnancy, the needs for iron rises, because a large portion of the mother's iron is used by the foetus, thus the possibility for anaemia is greater. Physically, anaemia is defined as a reduction in the blood's capacity to transfer oxygen, and the consequent tissue hypoxia (Breymann 2015). Anaemia defines the reduction of the total quantity of the Hb in relation to the normal, physiological values of Hb < 12 g/dL) for females and Hb < 13 g/dL for males . The pregnant female loses approximately 800 mg iron and her body needs to replenish the lost amount of iron by consuming 2.8-6 mg iron per day. During the period of the first trimester the body's iron reserves are low, while during the second, these reserves are lowered further, whereas in the third trimester, after the iron-deficiency anaemia a reduction of the other iron-containing proteins may be observed. Reduction of the activity of iron-containing enzymes results with organic cellular changes leading to other symptoms related to anaemia. The symptoms of anaemia are manifested when the amount of Hb is reduced to < 75-80 g/L. Iron deficiency may be the reason for the appearance of the Immunodeficiency Syndrome. Pregnancy anaemia may be a soft state and it can be treated with ease if it is discovered in its initial phases. However, it can also be life-threatening for the mother and the foetus if it is not treated. The most severe anaemia, may present with a high risk of *exitus lethalis* for the mother and the fetus. **Anaemia diagnosis**: The signs of anaemia and bleeding, and the characteristics of peripheral blood samples, are sufficient elements for diagnosing anaemia, and beginning of its treatment.

Anaemia diagnosis is best verified by examination of the haematologic biomarkers (Er, Hb, Htc, Fe, MCV, MCH, and MCHC). The success of treatment of pregnancy anaemia is due to the increase of the observed reticulocytes in 7-12 days. The increase of Hb is observable only one week after beginning of treatment, whereas its values normalise only two months after beginning of the treatment, if the treatment adjusts well to the patient.

Treatment of anaemia: pregnancy anaemia can be easily treated by increasing the amount of iron consumption in form of tablets or iron-rich nutrients. Typically, this is the fundamental postulate for correction of pregnancy anaemia. However, in very rare cases, females suffering from severe anaemia may need blood transfusion. Iron rich medicaments may be administrated in oral, parenteral, and intravenous forms. The pregnant females require an increased amount of iron of 2 mg/day for the first trimester, 4 mg/day in the second trimester, and a minimal amount of 4-6 mg/day in the third trimester. The facts that the requirements for iron during pregnancy cannot be met only by nutrients, fruits and vegetables, even by optimal consumption, are well documented, if the pregnancy begins with a reduced and insufficient iron reserves. Thus, a female must begin the pregnancy with iron reserves of ≥300 mg. In fact, a study that evaluated the status of iron during the early pregnancy in females with iron reserves of <12 µg/L, showed that they had a higher predisposition to manifest anaemia, in relation to the females who began the pregnancy with concentration of iron above 12-14 µg/L, regardless of their iron consumption.

CONCLUSION

In conclusion we prefer that prevention and correction of pregnancy anaemia be treated with consumption of meat, fruits and vegetables rich-in-iron. If these recommendations do not show the positive, expected, effects within two-three weeks than treatment with iron-supplementary preparations should begin, in oral, parenteral, or intravenous form. It is recommended that a pregnant female consume a minimal amount of 30-40 mg of iron, folic acid and vitamin B12per day. In our research, administration of 30 – 60 mg iron per day in all of the pregnant females showed extremely positive effects in correction of anaemia without side effects. Thus, we prefer a follow-up of the iron reserves by testing of the haematologic biomarkers, to be the first step of the gynaecologists, because only than the symptoms of anaemia may be detected and the positive effects of the medicament therapy will be best appreciated.

REFERENCES

[1]. Health Organization. Iron Deficiency Anaemia: Assessment, Prevention and Control: A Guide for Programme Managers. Geneva, Switzerland: World Health Organization; 2001.

[2]. WHO. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Vitamin and Mineral Nutrition Information System. Geneva, Switzerland*:* World Health Organization*;*2011.

[3]. Stevens GA et al. Nutrition Impact Model Study Group (Anaemia). Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995-2011: a systematic analysis of population-representative data. *Lancet Glob Health.* 2013*;*1*(*1*):* e16-e25.

[4]. de Sá SA, Willner E, Duraes Pereira TA, de Souza VR, et al.Anemia in pregnancy: impact on weight and in the development of anemia in newborn. *Nutr Hosp.*2015*;*32*(5):*2071-2079.

[5]. Geng F, Mai X, Zhan J, et al. Impact of fetal-neonatal iron deficiency on recognition memory at 2 months of age. *J Pediatr.* 2015*;*167*(6):*1226-1232.

[6]. Scholl TO. Maternal iron status: relation to fetal growth, length of gestation, and iron endowment of the neonate. *Nutr Rev.* 2011*;*69*(*suppl 1*):*S23-S29.

[7]. Bothwell TH. Iron requirements in pregnancy and strategies to meet them. *Am J Clin Nutr.*2000*;*72*(*suppl 1*):*257S-264S.

[8]. Romslo I, Haram K, Sagen N, Augensen K. Iron requirement in normal pregnancy as assessed by serum ferritin, serum transferrin saturation and erythrocyte protoporphyrin determinations. *Br J ObstetGynaecol.* 1983*;*90*(*2*):*101-107.
[9]. Camaschella C. Iron-deficiency anemia. *N Engl J Med.* 2015*;*372*(*19*):*1832-1843.
[10]. Moretti D, Goede JS,et al. Oral iron supplements increase hepcidin and decrease iron absorption from daily or twice-daily doses in iron-depleted young women. *Blood.*2015*;*126*(*17*):*1981-1989.
[11]. Breymann C.Iron Deficiency Anemia in Pregnancy.SeminHematol. 2015 Oct;52(4):339-47.doi: 10.1053/j.seminhematol.2015.07.003. Epub 2015 Jul 10