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ORIGINAL RESEARCH

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Prognosis of iron deficiency anemia in pregnant women with different somatotypes

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BACKGROUND: Anemia during pregnancy, undiagnosed and untreated promptly, is the cause of various obstetric complications: spontaneous miscarriages, premature birth, placental insufficiency, obstetric bleeding, ante- and intrapartum fetal death.

AIM: The aim of this study was to evaluate the incidence of iron deficiency anemia in pregnant women with different somatotypes and to develop a prognostic model for the pathology onset.

MATERIALS AND METHODS: We examined 390 pregnant women. Somatometry was performed according to the method of R.N. Dorokhov in terms of pregnancy not exceeding 9-10 weeks. Of the examined pregnant women, 110 were of the macrosomatotype, 173 of the meso- and 107 of the microsomatotype. In a clinical blood test, the levels of hemoglobin and red blood cells were determined using well-known methods. Blood iron levels were evaluated by the colorimetric method with ferrozine using a Parma Iron Reagents Kit (Parma Diagnostics Ltd., Russia). Serum hepcidin levels were determined spectrophotometrically using ELISA methods.

RESULTS: Iron deficiency anemia was most commonly detected in pregnant women of the macro- and microsomatotype, when compared to those of the mesosomatotype (p < 0.05). There was no severe anemia in the study groups. The levels of hematological parameters (serum iron and serum hepcidin) were significantly higher in the group of pregnant women with latent anemia, compared to the study group without signs of anemia (p < 0.05). In the second trimester, iron deficiency anemia occurred in the group of patients with latent anemia. Using multiple regression analysis, a formula was obtained for predicting the onset of iron deficiency anemia in pregnant women of different somatotypes.

CONCLUSIONS: Hematological parameters (serum iron and serum hepcidin) should be attributed to markers of iron deficiency anemia and timely predict the onset of pathology. The mathematical formula obtained allows predicting with high accuracy the onset of iron deficiency anemia in pregnant women, taking into account the somatotype in the first trimester of pregnancy, and timely preventing the onset of pathology.

Keywords: somatotype; iron deficiency anemia; pregnancy; risk prediction.

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Прогноз железодефицитной анемии у беременных с разными соматотипами

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Обоснование. Анемия во время беременности, не диагностированная и не леченная своевременно, служит причиной различных акушерских осложнений — самопроизвольных выкидышей, преждевременных родов, нарушения кровообращения в маточно-плацентарно-плодовой системе, акушерских кровотечений, анте- и интранатальной гибели плода.

Цель — изучить частоту железодефицитной анемии у беременных с учетом типа конституции и разработать прогностическую модель возникновения данной нозологии.

Материалы и методы. Обследовали 390 беременных. Соматометрию проводили по способу Р.Н. Дорохова в сроках беременности, не превышающих 9–10 нед. Из наблюдаемых беременных 110 являлись представителями макросоматотипа, 173 — мезо- и 107 — микросоматотипа. Определяли уровни гемоглобина и эритроцитов по известным методикам. Содержание железа в крови оценивали колориметрическим способом с феррозином при помощи набора реагентов «Железо Парма» (000 «Парма Диагностика»). Гепцидин в сыворотке крови определяли спектрофотометрически методом ELISA.

Результаты. Железодефицитная анемия наиболее часто встречалась при беременности у представительниц макро- и микросоматотипа в сравнении с мезосоматотипами (p < 0.05). Анемии тяжелой степени в наблюдаемых группах не было. Концентрация гематологических показателей (железо и гепцидин в сыворотке крови) была значительно выше в группе беременных со скрытым течением анемии в сравнении с группой без признаков анемии (p < 0.05). Во II триместре у женщин группы со скрытым течением возникла железодефицитная анемия. При помощи множественного регрессионного анализа получена формула для прогноза наступления железодефицитной анемии у беременных разных соматотипов.

Заключение. Гематологические показатели (железо и гепцидин в сыворотке крови) следует относить к маркерам железодефицитной анемии и своевременно прогнозировать наступление патологии. Математическая формула позволяет с высокой точностью определить наступление железодефицитной анемии у беременных с учетом типа конституции в I триместре беременности и предупредить развитие патологии.

Ключевые слова: соматотип; железодефицитная анемия; беременность; прогнозирование риска.

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BACKGROUND

The impact of various comorbidities on the course of a pregnancy frequently has a negative impact on both the fetus and the mother. Anemia during pregnancy is no exception, and it is still one of the leading causes of maternal and perinatal morbidity around the world. Thus, in more than 80% of the countries in the world, the incidence of iron deficiency anemia during pregnancy exceeds 20%. Several authors estimate that the global prevalence of anemia in pregnant women is approximately 41%. Further, undiagnosed and untreated anemia during pregnancy leads to a variety of obstetric complications, such as spontaneous miscarriages, premature delivery, circulatory disorders in the uteroplacental-fetal system, obstetric bleeding, and ante- and intranatal fetal death. Moreover, individual works in the current scientific literature pay increasing attention to the peptide hormone hepcidin in the diagnostics of anemia. Hepcidin is involved in the regulation of systemic iron metabolism, which is implemented through iron absorption from the intestinal walls, as well as by its release in liver cells and macrophages. With an increase in the blood concentration of iron, more hepcidin is synthesized in the liver cells, causing the degradation of the ferroportin protein in the target cells, whereas ferroportin promotes the entry of iron ions into the blood. Thus, when the concentration of iron in the blood increases, so does the concentration of hepcidin, which prevents the blood level of iron from increasing further. Iron, as is well known, causes cell damage at high concentrations. With a decrease in the blood concentration of iron, hepcidin is less secreted in hepatocytes, while ferroportin promotes iron absorption from enterocytes and its entry into the blood. In modern scientific research, the search for new predictors for the timely prevention of pathological processes is receiving increasing attention. Given the significant adverse effects of pregnancy anemia on maternal and fetal outcomes, it is critical to detect and prevent this clinical condition as early as possible [1-6].

Many published scientific studies have found a correlation between constitutional aspects and the occurrence of various pathological conditions and diseases [7–11]. For the purpose of somatotyping, many scientific works in recent decades have used R.N. Dorokhov's classification and methodology. The author divides the constitution into two parts: general and particular. This technique is applicable for both adults and children and adolescents, and when assessing morphometric characteristics, not only dimensional variation but also the components of weight and proportional development are assessed, and the terms "somatotype" and "constitution" are identical [12, 13].

There are not enough scientific studies looking into the relationship between constitutional aspects and the onset of iron deficiency anemia during pregnancy.

The goal of the study was to analyze the prevalence of iron deficiency anemia in pregnant women, taking into account the type of constitution, and to develop a prognostic model for the onset of this nosology.

MATERIALS AND METHODS

A total of 390 pregnant women were examined. In terms of pregnancy not exceeding 9–10 weeks, somatometry was performed using R.N. Dorokhov's method. Among those examined, 110 pregnant women belonged to the macrosomatotype, 173 to the mesosomatotype, and 107 to the microsomatotype [12, 13]. The study included pregnant women with a gestational age of less than 9–10 weeks at the time of inclusion in the study, a singleton pregnancy, and no history of severe somatic pathologies, after signing an informed consent to participate in the study.

All subjects had a clinical blood test at 9–10 weeks of gestation and again at 21–22 weeks; the concentration of hemoglobin and erythrocytes was determined using the conventional methods [14]. During the same period of pregnancy, the concentration of iron and hepcidin in the blood serum was assessed. Blood, taken in the morning on an empty stomach in a Vacutainer tube (with a clotting activator and a separating gel), was incubated for 30 min at +20 to +25°C, which corresponds to room temperature, before centrifugation for 10 min at 3000 rpm. The blood iron level was determined using the colorimetric method with ferrozine and a set of Parma Iron reagents. Serum hepcidin was assessed spectrophotometrically by ELISA. Moreover, human Hepc25 (Hepcidin 25) ELISA Kit (Elabscience Biotechnology) was used.

For mathematical data processing, the STATGRAPHICS Plus 5.0 and SPSS 15.0 programs were used. The data were presented in the form of an arithmetic mean and a mean error. To determine whether the distribution of indicators corresponded to the law of normal distribution, the Shapiro—Wilk test was used. With normal distribution of attributes, multiple regression analysis was carried out. In addition, the student's *t*-test was used to identify differences in groups.

RESULTS AND DISCUSSION

In the pregnant women examined, 60% of the women were primiparous, while 40% were multiparous. The age of the pregnant women ranged from 18 to 38 years (average age was 27.5 ± 2.8 years).

Iron deficiency anemia was most often detected in representatives of the macro- and microsomatotypes during pregnancy than in those with mesosomatotype (p < 0.05) (Table 1). Severe anemia was not found in any of the groups.

The concentration of hematological parameters (blood iron and hepcidin) was significantly lower in the group of

pregnant women with a latent course of anemia compared to the group without signs of anemia (p < 0.05) (Table 2, Figs. 1 and 2), and their level continued to decrease in the second trimester of gestation. In a group of women with a latent course in the second trimester, iron deficiency anemia developed.

During pregnancy, under the influence of hormones, the motility of the gastrointestinal tract changes, as does the absorption of products, including trace elements, and iron is redistributed in favor of the fetus, thereby reducing the level of iron in the blood, which leads to a decrease in the synthesis of hepcidin in hepatocytes and, as a result,

Table 1. Incidence of iron deficiency anemia in the pregnant women examined

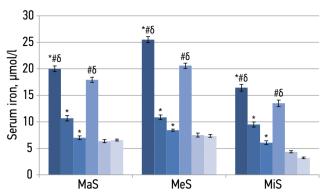
	Somatotype						
Groups of pregnant women	MaS (n = 110)		MeS (n = 173)		MiS (n = 107)		
	n	%	n	%	n	%	
With iron deficiency anemia	15#	13.6	15	8.7	24*	22.4	
With mild anemia	13#	11.8	15	8.7	20*	18.7	
With moderate anemia	2	1.8	-	-	4	3.7	
With severe anemia	_	_	_	_	_	_	

Note. MaS, macrosomatotype; MeS, mesosomatotype; MiS, microsomatotype. * differences between MeS and MiS somatotypes are statistically significant (p < 0.05); * differences between MaS and MiS somatotypes are statistically significant (p < 0.05).

Table 2. Hematological parameters in the women examined

C	la dia sasa		Somatotype					
Groups	Indicator	MaS (n = 110)	MeS (n = 173)	MiS (n = 107				
	9–10 weeks o	f pregnancy						
Pregnant women without anemia	Erythrocytes, ×10 ¹² /l	4.5 ± 0.02	4.7 ± 0.05	4.4 ± 0.07				
	Hemoglobin, g/l	128.2 ± 1.3	129.4 ± 1.4	125.4 ± 1.6				
	Serum iron, µmol/l	20.3 ± 0.6	25.8 ± 0.6** 16.7 ± 0					
	Serum hepcidin, ng/ml	67.7 ± 1.1*	77.7 ± 1.2**	58.3 ± 1.4				
Pregnant women with latent course of anemia	Erythrocytes, ×10 ¹² /l	4.03 ± 0.04	4.13 ± 0.07	3.97 ± 0.05				
	Hemoglobin, g/l	121.5 ± 1.4	122.2 ± 1.3	120.5 ± 1.7				
	Serum iron, µmol/l	$10.8 \pm 0.6^{\delta}$	$10.9 \pm 0.5^{\delta}$	$9.6\pm0.2^{\delta}$				
	Serum hepcidin, ng/ml	$20.3 \pm 1.2^{\delta}$	24.8 \pm 0.8**. δ	$19.2 \pm 0.7^{\delta}$				
Pregnant women with anemia	Erythrocytes, ×10 ¹² /l	$3.58 \pm 0.05^{\delta\delta}$	$3.65\pm0.05^{\delta\delta}$	$3.45 \pm 0.04^{\circ}$				
	Hemoglobin, g/l	102.6 \pm 1.5 $^{\delta\delta}$	104.2 ± 1.3**. δδ	97.1 ± 1.6 ^{δδ}				
	Serum iron, µmol/l	$7.3 \pm 0.06^{*.\delta\delta}$	8.5 \pm 0.08**. $\delta\delta$	$6.3 \pm 0.1^{\delta\delta}$				
	Serum hepcidin, ng/ml	$9.5 \pm 0.06^{*.6\delta}$	12.6 \pm 0.07**. $\delta\delta$	$7.4 \pm 0.09^{\delta\delta}$				
	21–22 weeks	of pregnancy						
Pregnant women without anemia	Erythrocytes, ×10 ¹² /l	4.4 ± 0.1	4.5 ± 0.08	4.1 ± 0.09				
	Hemoglobin, g/l	122.3 ± 1.7	123.6 ± 1.6 120.3 ±					
	Serum iron, µmol/l	18.1 ± 0.2*	20.6 ± 0.4**	13.6 ± 0.6				
	Serum hepcidin, ng/ml	59.4 ± 1.3	67.4 ± 1.4**	54.1 ± 1.1				
Pregnant women with latent course of anemia	Erythrocytes, ×10 ¹² /l	$3.61 \pm 0.09^{\delta}$	$3.68\pm0.07^{\delta}$	3.42 ± 0.06				
	Hemoglobin, g/l	$104.4 \pm 1.6^{\text{\#.}\delta}$	105.3 \pm 1.8 ^{#. δ}	99.2 ± 1.9#.				
	Serum iron, µmol/l	$6.3 \pm 0.08^{\text{\#.} \delta}$	$7.4 \pm 0.09^{\delta}$	$4.2 \pm 0.06^{\delta}$				
	Serum hepcidin, ng/ml	$8.3 \pm 0.5^{\text{\#.}\delta}$	10.2 \pm 0.7 **. #. δ	5.2 ± 0.8 ^{#. 8}				
Pregnant women with anemia	Erythrocytes, ×10 ¹² /l	$3.47 \pm 0.1^{\delta\delta}$	$3.51 \pm 0.2^{\delta\delta}$	$3.32 \pm 0.4^{\delta\delta}$				
	Hemoglobin, g/l	$98.7 \pm 1.4^{\delta\delta}$	101.7 ± 1.6**. δδ	94.3 ± 1.8 ^{δδ}				
	Serum iron, µmol/l	$6.6 \pm 0.06^{\delta\delta}$	$7.4 \pm 0.07^{**.\delta\delta}$	3.2 ± 0.07^{66}				
	Serum hepcidin, ng/ml	$7.3 \pm 0.08^{\star.\delta\delta}$	10.3 \pm 0.07**. $\delta\delta$	4.3 ± 0.04^{86}				

Note. MaS, macrosomatotype; MeS, mesosomatotype; MiS, microsomatotype. *differences between MaS and MiS are statistically significant (p < 0.05); ** differences between indicators at a gestational age of 9–10 and 21–22 weeks (p < 0.05); * 5 differences between the groups of pregnant women without anemia and those with a latent course of anemia (p < 0.05); 5 differences between the groups of pregnant women without anemia and those with anemia (p < 0.05).



- Pregnant women without anemia (9–10 weeks)
- Pregnant women with latent course of anemia (9–10 weeks)
- Pregnant women with anemia (9–10 weeks)
- Pregnant women without anemia (21–22 weeks)
- Pregnant women with latent course of anemia (21–22 weeks)
- Pregnant women with anemia (21–22 weeks)

Fig. 1. Concentration of serum iron in the groups under study. MaS, macrosomatotype; MeS, mesosomatotype; MiS, microsomatotype. * differences between indicators in the gestational age of 9–10 and 21–22 weeks (p < 0.05); * differences between the groups of pregnant women without anemia and those with a latent course of anemia (p < 0.05); * differences between the groups of pregnant women without anemia and those with anemia (p < 0.05)

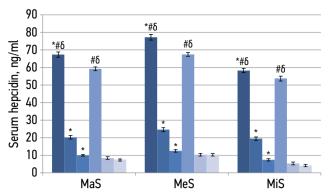
a decrease in its level in the blood. Latent anemia develops, resulting in a hypoxic state in various organs and systems, including the intestinal walls, which aggravates the processes of iron absorption. With a prolonged course of hypoxia, the concentration of iron and hepcidin in the blood continues to decrease, and anemia develops with clinical manifestations.

All of the above confirms that hematological parameters (blood serum iron and hepcidin) should be attributed to markers of iron deficiency anemia, allowing for the timely detection of a latent pathological process (anemia), predicting the onset of pathology, and influencing the links of a vicious circle, thereby preventing the progression of anemia.

Correlation and regression analysis using the SPSS program revealed a correlation between iron deficiency anemia and somatotype (r=-0.85; p<0.05), fatty component (r=0.91; p<0.05), muscle component of weight (r=-0.87; p<0.05), serum iron concentration (r=-0.96; p<0.05), and serum hepcidin concentration (r=-0.88; p<0.05) in pregnant women. These indicators were consistent with the normal distribution law. The close relationship between the listed indicators and their correspondence to the normal distribution allowed for a development of a prediction formula during the process of multiple regression analysis:

POIDA =
$$188.96 + (25.01 \cdot A) - (0.86 \cdot B) - (1.36 \cdot C) - (2.55 \cdot D) - (0.96 \cdot E),$$

where POIDA is the probability of onset of iron deficiency anemia (%), A the points of somatotyping, B the fatty component



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- Pregnant women without anemia (9–10 weeks)
- Pregnant women with latent course of anemia (9–10 weeks)
- Pregnant women with anemia (9–10 weeks)
- Pregnant women without anemia (21–22 weeks)
- Pregnant women with latent course of anemia (21–22 weeks)
- Pregnant women with anemia (21–22 weeks)

Fig. 2. Concentration of serum hepcidin in the examined groups. MaS, macrosomatotype; MeS, mesosomatotype; MiS, microsomatotype. * differences between indicators in the gestational age of 9–10 and 21–22 weeks (p < 0.05); * differences between the groups of pregnant women without anemia and those with a latent course of anemia (p < 0.05); * differences between the groups of pregnant women without anemia and those with anemia (p < 0.05)

of weight (%), C the muscle component of weight (%), D the concentration of iron in the blood serum (μ mol/l), and E the concentration of hepcidin in the blood serum (μ mol/l).

In the regression formula, the indicators of a pregnant woman should be substituted. According to well-known scales, a result of 60% or higher indicates a high risk of iron deficiency anemia; a result of 30–60% indicates a moderate risk; and a result of less than 30% indicates a low risk [15].

An example of calculating the probability of the onset of iron deficiency anemia 1. Pregnant woman D, 27 years old, at a gestational age of 6 weeks, with somatometry according to R.N. Dorokhov technology, had a height of 159.3 cm, a weight of 49.2 kg, a fat mass of 11.79 kg (24.2%), and a muscle mass of 19.79 kg (40.5%). Pregnant woman D had a microsomatotype (0.382 points). At the gestational age of 9 weeks, the iron concentration in the blood serum was 22.6 umol/l, the blood serum hepcidin was 66.9 ng/ml, the erythrocyte level was $4.57 \cdot 10^{12}$ /l, and the blood hemoglobin was 123.8 g/l. Moreover, the probability of the onset of iron deficiency anemia was 1.5%. During this pregnancy, the female patient did not develop iron deficiency anemia during the follow-up, confirming the correctness of the POIDA calculation according to the equation.

An example of calculating the probability of the onset of iron deficiency anemia 2. Pregnant woman S, 26 years old, at a gestational age of 7 weeks, with somatometry according to R.N. Dorokhov technology, had a height of 177.4 cm, a weight of 86.2 kg, a fat mass of

26.69 kg (31.2%), and a muscle mass of 33.79 kg (39.2%). Pregnant woman S had a macrosomatotype (0.678 points). At a gestational age of 10 weeks, the iron concentration in the blood serum was 8.5 μ mol/l, the blood serum hepcidin was 8.1 ng/ml, the erythrocyte level was $4.04 \cdot 10^{12}$ /l, and the hemoglobin was 122.8 g/l. Moreover, the probability of the onset of iron deficiency anemia was 96.9%. During this pregnancy, the female patient did not develop iron deficiency anemia during the follow-up in the second trimester (mild anemia), confirming the correctness of calculating the probability of iron deficiency anemia using the formula.

CONCLUSIONS

In pregnant women with macro- and microsomatotypes, the risk of iron deficiency anemia is higher compared than in pregnant women with the mesosomatotype. Hematological parameters (iron and hepcidin in the blood serum) should be classified as markers of iron deficiency anemia; their use can predict the onset of pathology in a timely manner. The mathematical equation allows for the accurate prediction of the onset of iron deficiency anemia in pregnant women, taking into account the constitutional aspects in the first trimester of pregnancy when registering in an antenatal clinic, and for the timely prevention of the onset of pathology.

ADDITIONAL INFORMATION

Conflict of interest. The authors declare no conflict of interest. **Funding.** The study had no external funding.

Compliance with the principles of ethics. The study was approved by the local ethical committee of the North Ossetian State Medical Academy of the Ministry of Health of Russia (protocol No. 5.7 dated 12/08/2015).

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