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Iron deficiency anemia in multiparous women: an analysis of clinical indicators of anemia treatment

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Aim – to compare the effectiveness of two therapeutic approaches for iron-deficiency anemia (IDA) in multiparous pregnant women: ferric iron (Fe^{3+}) preparations alone and ferrous iron (Fe^{2+}) salts combined with a vitamin-mineral complex, by evaluating pregnancy complications, delivery outcomes, and early neonatal status according to anemia severity and trimester of pregnancy.

Materials and methods. The study included 100 pregnant women with three or more pregnancies. The Comparison group included 40 pregnant women with IDA who received only ferric iron supplements. The Main group included 60 pregnant women with IDA who received treatment with ferrous iron salts (in combination with a vitamin-mineral complex).

Results. When comparing the Comparison group with the Main group, complications such as threatened miscarriage and chronic intrauterine hypoxia of the fetus were significantly more common in the former group. Significant differences in the incidence of complications such as premature rupture of membranes (PROM) and hypotonic labor were also observed during childbirth, depending on the severity of anemia and the trimester of pregnancy. According to the results, grade II anemia in the third trimester is associated with significantly higher rates of threatened miscarriage, chronic inflammatory heart failure, PROM, and lower neonatal Apgar scores. The clearest differences were observed among women with grade II anemia in the third trimester: threatened miscarriage was recorded in 63.6% versus 0.0%, CFIH in 45.5% versus 0.0%, and PROM in 54.5% versus 10.5% in the Comparison and Main groups, respectively.

Conclusion. Thus, the administration of ferrous iron salts in combination with a vitamin-mineral complex not only improved women's quality of life but also reduced the incidence of several obstetric complications during pregnancy and childbirth.

The study was conducted in accordance with the principles of the Declaration of Helsinki. Informed consent from women was obtained for the study. The author declares no conflict of interest.

Keywords: iron-deficiency anemia, pregnancy, multiparous women, iron supplements, vitamin-mineral complex.

Залізодефіцитна анемія у жінок, які багато народжували: аналіз клінічних показників лікування анемії

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Мета – порівняти ефективність двох терапевтичних підходів до лікування залізодефіцитної анемії (ЗДА) у повторнородних вагітних: препаратів тривалентного заліза окремо та солей двовалентного заліза у поєднанні з вітамінно-мінеральним комплексом, оцінюючи ускладнення вагітності, результати пологів та ранній неонатальний стан залежно від тяжкості анемії та триместру вагітності.

Матеріали та методи. У дослідженні взяло участь 100 вагітних жінок із трьома або більше вагітностями. Групу порівняння становили 40 вагітних жінок із ЗДА, які отримували лише добавки тривалентного заліза. До основної групи увійшло 60 вагітних жінок із ЗДА, які отримували лікування солями двовалентного заліза (у поєднанні з вітамінно-мінеральним комплексом).

Результати. Під час співставлення груп порівняння та основної, такі ускладнення, як загроза викидня та хронічна внутрішньоутробна гіпоксія плода були значно частішими в групі порівняння. Значні відмінності в частоті таких ускладнень, як передчасний розрив плодових оболонок (ПРПО) та гіпотонічні пологи, також спостерігалися під час пологів, залежно від тяжкості анемії та триместру вагітності. Згідно з результатами, анемія II ступеня у третьому триместрі пов'язана зі значно вищими показниками загрози викидня, хронічної запальної серцевої недостатності, ПРПО та нижчих балів за шкалою Апгар у новонароджених. Найбільш чіткі відмінності спостерігалися у жінок із анемією II ступеня у третьому триместрі: загроза викидня була зареєстрована у 63,6% проти 0,0%, хронічна запальна серцева недостатність – у 45,5% проти 0,0%, а ПРПО – у 54,5% проти 10,5% у групі порівняння та основній групі відповідно.

Висновок. Введення солей двовалентного заліза в поєднанні з вітамінно-мінеральним комплексом не тільки покращило якість життя жінок, але й зменшило частоту виникнення кількох акушерських ускладнень під час вагітності та пологів.

Дослідження проведено відповідно до принципів Гельсінської декларації. Для проведення дослідження було отримано інформовану згоду жінок. Автор заявляє про відсутність конфлікту інтересів.

Ключові слова: залізодефіцитна анемія, вагітність, багатоплідні жінки, добавки заліза, вітамінно-мінеральний комплекс.

Anemia is one of the most common hematological abnormalities encountered by hospital physicians and practitioners. Globally, anemia affects

approximately 6 million people. The diagnosis of anemia is established based on hemoglobin (Hb) concentration determinations; however, this data

does not allow one to determine the underlying cause of the anemic condition [8].

Iron-deficiency anemia (IDA) manifests as hypoxic and sideropenic syndromes. Hypoxic syndrome includes all anemic symptoms: pale skin and visible mucous membranes, tachycardia, tinnitus, headaches, and weakness. Sideropenic symptoms include taste perversion, dry skin, nail changes, hair loss, stomatitis, tongue irritation, and dyspeptic symptoms [6].

IDA in pregnant women can lead to a number of complications for both the mother and fetus, including premature birth [7], placental insufficiency, threatened miscarriage (TM), infections, fetal malnutrition, and other complications. Anemia typically worsens with repeated pregnancies [9].

Frequent births and high parity reduce the vitality of women of active reproductive age. Multiparous women still account for a significant proportion of women of reproductive age [2]. Considering the above, as well as the high prevalence of IDA among this group of women, we conducted this study.

The aim of the study was to compare the effectiveness of two therapeutic approaches for IDA in multiparous pregnant women: ferric iron (trivalent iron, Fe^{3+}) preparations alone and ferrous iron (divalent iron, Fe^{2+}) salts combined with a vitamin-mineral complex, by evaluating pregnancy complications, delivery outcomes, and early neonatal status according to anemia severity and trimester of pregnancy.

Materials and methods of the study

The study included 100 pregnant women. It was conducted among women who visited Maternity Hospital No. 5 named after Shamama Aleskerova at the Department of Obstetrics and Gynecology II of the Azerbaijan Medical University between 2018 and 2023.

According to the World Health Organization classification of Hb concentration, the degree of anemia was determined as follows: Grade I – Hb 100–110 g/L; Grade II – Hb 70–99 g/L; Grade III – Hb below 70 g/L.

Among the examined pregnant women, the Comparison group included 40 women with anemia who received only ferric iron supplements. The Main group included 60 pregnant women with IDA who received treatment with ferrous iron salts in combination with a vitamin and mineral supplement. All percentages in the text and tables were recalculated and are presented from the denominator indicated for the relevant treatment group or subgroup. Thus,

for subgroup analyses, the denominator is the number of women in that subgroup, not the number of patients with a single clinical sign.

Hemogram was determined using a Mythic 18 hematology analyzer (Switzerland), serum iron levels were determined biochemically using a Human Diagnostics (Germany) Chromazurol assay (CAB), and serum ferritin was measured by Enzyme-Linked Immunosorbent Assay (ELISA) using a «Pishtaz Teb» (Islamic Republic of Iran) assay.

Statistical methods. The results were analyzed using the Mann-Whitney U test and analysis of variance (ANOVA) in the SPSS-26 statistical package. The statistical significance of differences between the group indicators was calculated using the Pt (Student's Bonferroni), $P\chi^2$ (Pearson), and PU (Mann-Whitney) criteria, with $p < 0.05$ considered statistically significant in the SPSS-26 program.

Results of the study and discussion

The study analyzed clinical outcomes of pregnancy and childbirth depending on the trimester of pregnancy and the degree of anemia.

Grade I anemia was detected in 12 of the women: the Comparison group included 5 women, and the Main group included 7 women.

Threatened miscarriage was observed in 2 (40.0%) patients in the Comparison group, while in the Main group no cases were noted – 0 (0.0%) ($P\chi^2=0.067$; $PU=0.079$). Chronic intrauterine hypoxia of the fetus (CIHF) was detected in 1 (20.0%) patient in the Comparison group and was not observed in the Main group – 0 (0.0%) ($P\chi^2=0.217$; $PU=0.237$). According to the severity of preeclampsia, in the Comparison group, preeclampsia was absent in 4 (80.0%) patients, moderate preeclampsia was not noted – 0 (0.0%), while severe preeclampsia was registered in 1 (20.0%) patient. In the Main group, preeclampsia was absent in all 7 (100.0%) patients; moderate and severe forms were not registered – 0 (0.0%) in both cases ($P\chi^2=0.217$; $PU=0.237$). Premature rupture of membranes (PROM) was observed in 4 (80.0%) patients in the Comparison group and was not noted in the Main group – 0 (0.0%) ($P\chi^2=0.004$; $PU=0.006$). Hypotonic labor was registered in 2 (40.0%) patients in the Comparison group, while in the Main group no cases were observed – 0 (0.0%) ($P\chi^2=0.067$; $PU=0.079$).

When assessing newborns using the Apgar score at the 5th minute, a score of 6 points was not recorded in either group. A score of 7 points was noted in 2 (40.0%) newborns in the Comparison group and

Table 1

Clinical features of pregnancy during the third trimester and Grade I anemia

Indicators		Groups					
		Comparison (n=5)		Main (n=7)			
		n	%	N	%	P χ^2	PU
TM	Absent	3	60.0	7	100.0	0.067	0.079
	Present	2	40.0	0	0.0		
CIHF	Absent	4	80.0	7	100.0		
	Present	1	20.0	0	0.0	0.217	0.237
Preeclampsia grade	Absent	4	80.0	7	100.0		
	Moderate	0	0.0	0	0.0		
	Severe	1	20.0	0	0.0	0.217	0.237
PROM	Absent	1	20.0	7	100.0		
	Present	4	80.0	0	0.0	0.004	0.006
Hypotonic labor	Absent	3	60.0	7	100.0		
	Present	2	40.0	0	0.0	0.067	0.079
Apgar score at the 5 th minute	6	0	0.0	0	0.0		
	7	2	40.0	0	0.0		
	8	3	60.0	7	100.0	0.067	0.079
Postpartum complications	Absent	4	80.0	7	100.0		
	Present	1	20.0	0	0.0	0.217	0.237

Notes: the statistical significance of differences between the group indicators: P χ^2 – by the Pearson Chi-square test; PU – by the Mann–Whitney U test.

was not recorded in the Main group – 0 (0.0%). A score of 8 points was recorded in 3 (60.0%) newborns in the Comparison group and in 7 (100.0%) newborns in the Main group (P χ^2 =0.067; PU=0.079). Postpartum complications were observed in 1 (20.0%) patient in the Comparison group and were not registered in the Main group – 0 (0.0%) (P χ^2 =0.217; PU=0.237).

The clinical analysis of the pregnancy course in the examined pregnant women with Grade I anemia in the third trimester of pregnancy is presented in Table 1.

When analyzing the indicators from Table 1, we revealed that Grade I anemia significantly elevates the risk of PROM and shows concerning trends for other perinatal complications. Severe preeclampsia, CIHF, and postpartum complications occurred only in the anemic group, though underpowered to confirm significance.

The clinical analysis of the pregnancy course in the examined pregnant women with Grade II anemia in the third trimester of pregnancy is presented in Table 2.

Among women with Grade II anemia (11 in the Comparison group and 19 in the Main group), TM was observed in 7 (63.6%) patients from the Com-

parison group, while in the Main group no cases were noted – 0 (0.0%) (P χ^2 =0.067; PU=0.000). CIHF was detected in 5 (45.5%) patients in the Comparison group and was not observed in the Main group – 0 (0.0%) (P χ^2 =0.217; PU=0.002). According to the severity of preeclampsia, in the Comparison group, preeclampsia was absent in 9 (81.8%) patients, moderate preeclampsia was registered in 2 (18.2%) patients, while severe preeclampsia was not noted – 0 (0.0%). In the Main group, preeclampsia was absent in all 19 (100.0%) patients; moderate and severe forms were not registered – 0 (0.0%) in both cases (P χ^2 =0.217; PU=0.059).

PROM was detected in 6 (54.5%) patients in the Comparison group and in 2 (10.5%) patients in the Main group (P χ^2 =0.004; PU=0.010). Primary hypotonic labor occurred more frequently in the Comparison group, where it was noted in 4 (36.4%) patients, whereas in the Main group it was registered in 2 (10.5%) patients (P χ^2 =0.067; PU=0.094). Assessment of the newborns using the Apgar score at the 5th minute revealed that a score of 6 points was recorded in 1 (9.1%) newborn in the Comparison group and was not recorded in the Main group – 0 (0.0%).

Table 2

Clinical features of pregnancy during the third trimester and Grade II anemia

Indicators		Groups					
		Comparison (n=11)		Main (n=19)			
		n	%	n	%	$P\chi^2$	PU
TM	Absent	4	36.4	19	100.0		
	Present	7	63.6	0	0.0	0.067	0.000
CIHF	Absent	6	54.5	19	100.0		
	Present	5	45.5	0	0.0	0.217	0.002
Preeclampsia grade	Absent	9	81.8	19	100.0		
	Moderate	2	18.2	0	0.0		
	Severe	0	0.0	0	0.0	0.217	0.059
PROM	Absent	5	45.5	17	89.5		
	Present	6	54.5	2	10.5	0.004	0.010
Hypotonic labor	Absent	7	63.6	17	89.5		
	Present	4	36.4	2	10.5	0.067	0.094
Apgar score at the 5 th minute	6	1	9.1	0	0.0		
	7	3	27.3	1	5.3		
	8	7	63.6	15	78.9		
	9	0	0.0	3	15.8	0.067	0.016
Postpartum complications	Absent	10	90.9	18	94.7		
	Present	1	9.1	1	5.3	0.217	0.690

Notes: the statistical significance of differences between the group indicators was determined by the following criteria: $P\chi^2$ – by the Pearson Chi-square test; PU – by the Mann–Whitney U test.

A score of 7 points was noted in 3 (27.3%) newborns in the Comparison group and in 1 (5.3%) newborn in the Main group. A score of 8 points was recorded in 7 (63.6%) newborns in the Comparison group and in 15 (78.9%) newborns in the Main group. A score of 9 points was not recorded in the Comparison group – 0 (0.0%), while in the Main group it was registered in 3 (15.8%) newborns ($P\chi^2=0.067$; $PU=0.016$). Postpartum complications were observed in 1 (9.1%) patient in the Comparison group and in 1 (5.3%) patient in the Main group ($P\chi^2=0.217$; $PU=0.690$).

According to the results, Grade II anemia in the third trimester is associated with significantly higher rates of TM, CIHF, PROM, and lower neonatal Apgar scores. Trends suggest a possible link to preeclampsia and hypotonic labor, though larger studies are needed for confirmation. No association was found between anemia and postpartum complications. Thus, vigilant monitoring and management of anemia in the third trimester are critical to mitigate risks of maternal (TM, CIHF, PROM) and neonatal (low Apgar) complications.

The clinical analysis of pregnancy progression in pregnant women with Grade III anemia in the third trimester is presented in Table 3.

According to the results, TM was recorded in all 3 (100.0%) patients in the Comparison group, whereas in the Main group it was observed in 2 (66.7%) patients. At the same time, in the Main group, TM was absent in 1 (33.3%) patient ($P\chi^2=0.273$; $PU=0.317$). CIHF was identified in all patients in the Comparison group and in 1 (33.3%) patient in the Main group. In the Main group, CIHF was absent in 2 (66.7%) patients ($P\chi^2=0.083$; $PU=0.114$). Regarding the severity of preeclampsia, all patients in the Comparison group had severe preeclampsia – 3 (100.0%). In the Main group, moderate preeclampsia was registered in 1 (33.3%) patient, and severe preeclampsia was not observed ($P\chi^2=0.050$; $PU=0.034$). PROM occurred in 2 (66.7%) patients in the Comparison group, while no cases were registered in the Main group – 0 (0.0%) ($P\chi^2=0.083$; $PU=0.114$).

Hypotonic labor was noted in 2 (66.7%) patients in the Comparison group and was not observed in

Table 3

Clinical features of pregnancy during the third trimester and Grade III anemia

Indicators		Groups					
		Comparison (n=3)		Main (n=3)			
		n	%	n	%	$P\chi^2$	PU
TM	Absent	0	0.0	1	33.3	0.273	0.317
	Present	3	100.0	2	66.7		
CIHF	Absent	0	0.0	2	66.7	0.083	0.114
	Present	3	100.0	1	33.3		
Preeclampsia grade	Absent	0	0.0	2	66.7	0.050	0.034
	Moderate	0	0.0	1	33.3		
	Severe	3	100.0	0	0.0		
PROM	Absent	1	33.3	3	100.0	0.083	0.114
	Present	2	66.7	0	0.0		
Hypotonic labor	Absent	1	33.3	3	100.0	0.083	0.114
	Present	2	66.7	0	0.0		
Apgar score at the 5 th minute	7	1	33.3	1	33.3	1.000	1.000
	8	2	66.7	2	66.7		
Postpartum complications	Нет	3	100.0	3	100.0		1.000
	Есть	0	0.0	0	0.0		

Notes: the statistical significance of differences between group parameters was determined using the following criteria: $P\chi^2$ – according to the Pearson Chi-square test; PU – according to the Mann–Whitney U test.

the Main group – 0 (0.0%). When evaluating newborns according to the Apgar score at the 5th minute, a score of 7 points was observed in 1 (33.3%) newborn in the Comparison group and in 1 (33.3%) newborn in the Main group. A score of 8 points was recorded in 2 (66.7%) newborns in the Comparison group and in 2 (66.7%) newborns in the Main group ($P\chi^2=1.000$; PU=1.000). Postpartum complications were not observed in either group.

The obtained results showed that Grade III anemia was associated with the highest clinical risk. Despite the very small sample size, severe preeclampsia occurred in all women of the Comparison group and in none of the women of the Main group, while moderate preeclampsia was noted in one woman in the Main group. TM, CIHF, PROM, and hypotonic labor remained more frequent in the Comparison group. The lack of a statistically significant difference for several outcomes should be interpreted cautiously because each subgroup included only three women. Nevertheless, the direction of the findings is consistent with Tables 1 and 2 and supports the clinical benefit of the combined therapeutic regimen.

During pregnancy, the impact of anemia on adverse maternal and fetal outcomes has been assessed. According to evidence-based medicine, adequate

treatment can achieve positive pregnancy outcomes [10]. In pregnant women with IDA, the incidence of miscarriage is 15–42%, premature birth – 11–42%, arterial hypotension – 40%, fetal hypoxia – 35%, premature placental abruption – 25–35%, development of preeclampsia – 29%, fetal malnutrition – 25%, impaired uterine contractility (weak labor, hypotension) – 10–15%, purulent-septic diseases of the postpartum period – 12%, bleeding in the third stage of labor and the early postpartum period – 10% [3,5,11].

J. Gurbanova et al. note that the incidence of anemia was 61.1% in women with preterm labor and in pregnant women with threatened preterm labor (the study group), compared to 52.5% in women without threatened preterm labor (the Control group) ($p=0.187$) [4]. In our study group, preterm birth in the Comparison group was 14.3%, which is also a significant figure.

The obtained results are consistent with published data indicating that IDA during pregnancy increases the risk of adverse maternal and fetal outcomes, including miscarriage, preterm birth, fetal hypoxia, preeclampsia, impaired uterine contractility, and postpartum complications [3–5,10,11]. In the present study, adverse outcomes were not distributed equally between therapeutic groups. The Fe^{3+} monotherapy group had higher rates of TM, CIHF,

PROM and hypotonic labor, while the Fe²⁺ plus vitamin-mineral complex group demonstrated fewer complications and better 5-minute Apgar scores in the subgroup with grade II anemia. Therefore, the study does not simply confirm the frequency of complications in IDA; it shows that the choice of correction regimen may influence the clinical course of pregnancy and childbirth in multiparous women.

A possible explanation is that Fe²⁺ salts in combination with micronutrient support may contribute to more effective restoration of iron metabolism and improvement of maternal adaptive capacity during pregnancy. Better correction of iron deficiency may reduce tissue hypoxia, improve placental function, and lower the probability of uterine contractility disorders. At the same time, the interpretation of subgroup results should consider the limited number of observations in some strata, especially in grade III anemia. Larger prospective studies are needed to verify these findings.

Thus, in patients with IDA, the administration of an effective iron supplement in combination with a vitamin and mineral complex helps prevent complications [1] associated with anemia during pregnancy (TM, chronic intrauterine fetal hypoxia, weak labor, etc.). This has a positive effect on the course of pregnancy and childbirth, helps to maintain the mother's health, improve her quality of life, and reduce the incidence of perinatal diseases in the fetus, thereby contributing to the health of future generations.

Conclusion

The administration of ferrous iron salts in combination with a vitamin and mineral complex not only improved women's quality of life but also reduced the incidence of several obstetric complications during pregnancy and childbirth.

The author declares no conflict of interest.

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