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Influence of Maternal Anemia During Pregnancy on Placenta and Newborns

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ABSTRACT

Introduction: Sideropenic anemia is a common pregnancy disorder. Depending on severity, maternal anemia can significantly influence morphometric characteristic of placental tissue, pregnancy course and outcome. Objectives: to estimate if maternal anemia a) results with significant placental changes; b) influence on newborn weight, length and vitality. **Patients, material and methods**: Research included 100 women and their newborns, 50 anemic, and 50 women in the control group. Sixty placentas were collected, placental mass and volume was determined, and blood vessels of terminal villi were stereologically analyzed. Newborns mass and body length, and Apgar scores within 1 and 5 minutes after delivery were recorded. **The results:** Placentas of anemic pregnant women showed significant increase of terminal villi blood vessels (224,18 vs. 197,00 cm^3; p<0,0001), but total placental mass and volume did not differ significantly. Anemic mothers' newborns were significantly shorter (51,76 vs. 55,54 cm; p<0,0001), smaller body mass (3048,00 vs. 3615,60 g; p<0,0001) and delivered one week early (38,2 vs. 39,2 GW; p<0,0001), but not significantly poorer vitality (p>0,05) comparing with the control group. **Conclusion:** Sideropenic anemia increase placental maturity, that could be a possible cause of earlier spontaneous delivery among anemic women. The anemic mothers' newborns are shorter and lower body mass, but not poorer vitality index.

Key words: Pregnancy anemia, Terminal villi blood vessels, Newborns.

1. INTRODUCTION

Sideropenic anemia is a common pregnancy disorder, with the incidence among pregnant women from 20 to 40% (1, 2). According to WHO, pregnancy anemia exists if hemoglobin (Hb) is lower than 110,00 g/l and hematocrit (Htc) lower than 0,31 (3). Rough estimate of hematological pregnant women's status imply checking of Hb and Htc values, that have been modulated by degree of pregnant woman blood volume enlargement (4).

The placenta plays an active role of fetal programming during intrauterine life (5), and placental maturity, with fully mature villous tree and increased capillarization, is required for spontaneous induction of labor (6). Specific pregnancy condition either increase placental mass, such as pregnancy diabetes or multiple pregnancies, or placental volume, such as maternal anemia or pregnancy at high altitude (7). The placenta acts uniquely as both a conduit of oxygen to the fetal circulation and a significant consumer of oxygen to support its own metabolism and competition between these two demands must be carefully managed, particularly when oxygen resources become limited (8). Amount of available oxygen is a critical factor in placental development and development of placental blood vessels as well (9).

Low Hb concentration during pregnancy is associated with increased risk for preterm delivery of low birth weight baby (10) with a significant decreased Apgar score value during the first and the fifth minute after delivery (11).

Purpose of research was to determine a) if the pregnancy anemia influences placental mass and volume, and terminal villis' blood vessels; b) if the anemic mothers deliver their babies earlier than the pregnant woman of the control group; c) if the newborns of the anemic mothers are lower birth weight, length and poor birth vitality compared to the control group.

2. PATIENTS, MATERIAL AND METHODS

This prospective research included 100 pregnant women and their newborns, delivered with vaginal delivery at Gynecology and obstetric Clinic, Tuzla. Data were collected by random choice method. The following data were collected: a) considering pregnant women: age, biochemical blood test, gestational age; b) newborns: body mass, body length, Apgar score within the 1st and 5th minute after delivery. Pregnant women were divided into two groups: 50 pregnant women with maternal sideropenic anemia and 50 pregnant women with no signs of sideropenic anemia, control group.

The including criteria: single-baby pregnancies, pregnancy without any other pathological disorder that could have influence on pregnancy outcome, pregnancy from

37th to 42nd gestational week, maternal age from 20 to 35 years, spontaneous vaginal delivery, Hb lower than 110 g/l in first and third, and lower than 105 g/l in the second trimester, and Htc lower than 0,33 in first and third trimester and lower than 0,32 in the second trimester of pregnancy.

The total of 60 placentas, 30 from anemic mothers and 30 belonging to the control group, were weighed and volume determined, and sterologically analyzed in order to estimate the influence of maternal sideropenic anemia on terminal villis' blood vessels. The placentas were released of amnion and umbilical cord, placental mass was recorded and volume was determined by the amount of displaced liquid. Tissue samples were chosen systematically and fixed in 10% formalin solution; thickness of sections was 8 μm and was stained with hematoxylin and eosine. Tissues were stereologically analyzed using a multipurpose test system M-42, on magnification 40x, using Nikon microscope, model SE. The following has been analyzed: volume density (Vd tvbv) and total volume (V tvbv) of terminal villi blood vessels of the anemic mothers' placentas and placentas belonging to the control group.

Newborns data

The exact gestational age of the pregnant woman was determined according to date considering the last menstrual cycles that have been later confirmed with ultrasound diagnostic procedure.

Body mass was measured immediately after delivery using mechanical weighing machine „Maxima", Celje, and values were recorded by the closest 10-grams values.

Body length of newborns was determined using tape measure immediately after delivery, from top of head to heel with completely extended legs and values were recorded to the nearest whole number.

The newborns' clinical finding was specified by estimating the Newborns' vitality index using the estimation method according to Virginia Apgar, during the first and fifth minute after delivery.

Data were analyzed using statistical program Arcus Quick-stat Biomedical. Mann Whitney U test (for significance of Apgar score in 5th minute) and Student t-test (all other variables) were used to determine the statistical significance of the results. Hypotheses were tested at the level of signification $\alpha = 0.05$, i.e. differences between samples will be considered as significant if $p<0.05$.

3. RESULTS

This research was performed on 100 pregnant women that have been divided into two groups: 50 pregnant woman with biochemical parameters of sideropenic anemia, based on Hb and Htc values, and 50 pregnant women with no signs of sideropenic anemia or any other pregnancy disorder that could affect expecting mothers and their newborns. The range and mean values of Hb and Htc among anemic pregnant women during each trimester are shown in Table 1.

Variable, n = 50	I trimester	II trimester	III trimester
Hb (g/l)	79,00–101,00/ ±91,63	71,00–100,00/ 89,53	63,00–100,00/ 88,43
Htc	0,25–0,32/ 0,29	0,23–0,31/ 0,28	0,22–0,31/ 0,27

Table 1. The range and mean value of Hb and Htc of anemic mothers during the pregnancy

A total of 60 placentas were collected, 30 from anemic expecting mothers and 30 from mothers of the control group. Placental mass and volume was recorded; compared data showed no significant difference between these two groups (Table 2). Stereological analysis of terminal villis' blood vessels, using a multipurpose test system M42 magnifying 40x, showed significant increase of volume density and total volume of blood vessels of terminal villi (Table 2).

The body mass of the newborns in the group of anemic mothers range from 2100,00 to 4100,00 g and in control group from 3100,00 to 4400,00 g. Anemic mothers' newborns are approximately 553,00 g easier comparing to the control group newborns. There were four low birth weight newborns in the group of anemic mothers. Body length of the newborns delivered by anemic mothers ranged from 41,00 cm to 55,00 cm, and in control group from 49,00 to 60,00 cm. Newborns of anemic mothers are 3,78 cm shorter compared to the newborns of the control group. Although the lowest gestational age, considering the research criteria, was 37 weeks of gestation, 26% deliveries of anemic mothers were in the 37th gestational week. The average gestational age at the moment of delivery among anemic mothers was 38,20 weeks and in control group 39,20 weeks, and anemic mothers deliver their babies one week earlier comparing with the control group.

Variable n=30	Anemic mothers $\bar{\chi}^{*} \pm SD^{**}$	Control group $\bar{\chi} \pm SD$	t test value; significance (p)
Placental mass (g)	440,96 ± 77,68	468,30 ± 75,57	t = 1,59; p>0,05
Placental volume (cm^3)	424,80 ± 79,44	456,63 ± 74,95	t = 1,38; p>0,05
Vd tvbv (mm^0)	0,53 ± 0,11	0,42 ± 0,12	t = 8,90; p<0,01
V tvbv (cm^3)	224,18 ± 66,59	197,00 ± 65,84	t = 4,28; p<0,0001

Table 2. The placental mass and volume, volume density of terminal villi blood vessels (Vd tvbv) and total volume of terminal villi blood vessels (V tvbv)

Variable n=50	Anemic mothers $\bar{\chi} \pm SD$	Control group $\bar{\chi} \pm SD$	test value; significance (p)
GA (weeks)	38,20 ± 0,95	39,2 ± 0,88	t = 5,46; p<0,0001
Body mass (g)	3048,00 ± 405,96	3615,60 ± 319,71	t = 7,76; p<0,0001
Body length (cm)	51,76 ± 2,82	55,54 ± 2,32	t = 7,31; p<0,0001
A.S. within 1st .min.	8,70 ± 0,61	8,80 ± 0,53	t = 1,22 ; p>0,05
A.S. within 5th min.	8,90 ± 0,30	8,94 ± 0,23	**z** = -1,37 ;p>0,05

Table 3. Gestational age (GA), body mass, body length of newborns, and Apgar score (A.S.) within the 1st and 5th minute after birth.. Legend: * $\bar{\chi}$–mean value; ** SD–standard deviation

Apgar score values within the first minute after birth, in both groups, were similar. The lowest value in both groups was 7 and the highest was 9. After the fifth minute, the lowest Apgar score value in both groups was 8 and the highest was 9. Mean values and standard deviations of the Apgar score during the first and fifth minute after delivery are provided in Table 3.

4. DISCUSSION

Placental morphometric analysis depends on many factors, such as the number of analyzed placentas, possible relation of anemia and malnutrition of expecting mother (12, 13). Ultrasound measurement of placental volume between the 11th and 13th gestational week showed no significant alterations among anemic expecting women (14). The placentas included in our research weighted from 275,00 g to 574,00 g. Such variations and partly opposite values are earlier recognized as possible and common among anemic mothers and maternal anemia, therefore, represents an independent risk factor for abnormal placental growth (11). Literature data indicate that the hypoxia, depending on duration time, primarily results with hypertrophy (15), but with pregnancy advance, changes implicate the placental growth restriction and development of small, hypotrophic placenta (16). Compared with our results, anemic mothers' placentas total volume is similar with placentas from high altitude pregnancies that have been considered as a preplacental hypoxic condition (17). Since we found no significant difference comparing total placental volume, we wonder if maternal anemia had any significant influence on placental structures, particularly on terminal villi blood vessels.

In hypoxic condition, placental blood vessels continue to develop with the branching mode of angiogenesis to the end of pregnancy, that results in short terminal villi with numerous cross sections of blood capillaries (14). Placental villi that develop in hypoxic condition show increase share of fetal capillaries, with no specific signs of proliferation and changes are the result of capillary dilatation (18). According to our results, the hypoxia, as a consequence of maternal sideropenic anemia, lead to significant increase of terminal villi blood vessels in 1 cm^3 of placental tissue and their total volume as well. The placenta and fetus grow interdependently and perceived placental changes seems to be a compensatory mechanism that develops in order to appease fetal needs in the disturbed intrauterine environment. On the other hand, increased capillarization, an indicator of fully placental maturity, is responsible in coincidence with extraplacental signals, for induction of labor, and majority of spontaneous preterm deliveries shows more advanced placental villus maturation (6). Earlier spontaneous delivery among anemic expecting mothers, is also mediated with hypoxic stress and the synthesis of placental corticotropine releasing hormone, a powerful stimulator for subsequent production of fetal cortisol. Fetal cortisol influence the pathways of progesterone, estrogen and miometrial smooth muscle cells' oxitocyn receptors, in a manner to comply with the conditions for cervical dilatation and contraction of myometrium (19).

The extent to which placental changes caused by maternal anemia affect fetal development, growth and pregnancy outcome is not clearly understood. The placenta remodel its metabolism to decrease oxygen consumption, probably by increasing ATP production via glycolysis, this process can maintain oxygen supply to the fetus, but is still associated as fetal hypoglycemia with possible growth restriction (7). The anemia can be a direct cause of deterioration of fetal growth due to lack of oxygen flow to placental tissue or can be an indirect indicator of maternal nutrition deficit (20). Another consequence, a diminished supply of fetal and placental tissue with iron, modulates placental expression of transferrin receptors due to fetal and placental needs (21). Several studies implicate that maternal pregnancy anemia represents a significant risk factor for low or lower birth weight (22), earlier delivery (10), or newborn anemia[23]. Severity of maternal anemia is also recognized as a very important risk factor for adverse pregnancy outcome (24). A study conducted in animal models, pregnant mice, defined iron deficiency as an exact cause for lower fetal brain iron levels, shorter length, and lower weight of animal models (25).

Maternal anemia caused by lack of iron, but not other etiology, in early pregnancy is double-sized risk for preterm delivery of small birth weight baby (20). There are opposite data from developing countries where, among well-nourished maternal population, lower iron status of expecting mothers was associated with a higher birth weight and a longer duration of pregnancy (26). The results of our research show that the anemic mothers' newborns weighted in average 3048,00 g and were 553,00 g easier compared to the newborns of the control group. Body mass of healthy term newborns born at the same County hospital, during the war (from 1992 to 1995 year) was 3200,00 g, before the war 3400 g and ten years after the war, 3500,00 g (27). It seams that pregnancy under specific nutritive, material and social-demographic conditions that exist during the war, is similar to the condition of sideropenic anemia that is often related with mild or moderate malnutrition.

The body length of newborns is less liable to changes compared to the body mass, because it is principally defined by genetic factors and less depends on nutritive supply (28). In iron-deficiency anemia, iron-dependent enzymes involved in metabolism of collagen and vitamin D might become inactive with abnormal bone growth (29). Continuous deficiency of iron among anemic expecting mothers included in our research resulted in a significant shortening of body length of newborns. Using Apgar score, we estimated vitality index of the newborns. Apgar score during the first minute represents the tolerance of baby in the delivery process and in the fifth minute represents information how well the baby is doing outside the womb (30). Therefore, Apgar score acts as a measure of momentary newborns vitality, and does not give us information about nutritive and oxygen supply during pregnancy.

5. CONCLUSION

Moderate maternal sideropenic anemia causes significant increase of terminal villi blood vessels and advanced

placental maturity that could be reason for earlier delivery among anemic expecting woman. Long lasting hypoxia, probably mediated by the metabolic pathways of glucose and iron-dependent enzymes, results with significantly lower birth weight and length of newborns of anemic mothers.

CONFLICT OF INTEREST: NONE DECLARED

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