ORIGINAL ARTICLE

HYPODYNAMIA AS A FACTOR MODIFYING FUNCTIONAL MORPHOLOGY OF HUMAN PLACENTA

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ABSTRACT

The aim: Study of the functional morphology of placenta in a sedentary lifestyle of a woman during pregnancy.

Materials and methods: Object of the study: placentas obtained as a result of deliveries at term from women, urban residents, aged 20–40 years old, leading a sedentary lifestyle, and patients with a sufficiently high level of physical activity, the criteria of which corresponded to WHO recommendations. Immunohistochemical and morphometric studies of the placentas were carried out, followed by statistical analysis

Results: Prerequisites for reducing the efficacy of the functioning of fetoplacental complex with a sedentary lifestyle were sclerosis, the formation of intervillous fibrinoid and fibrinoid substitution of terminal villi. The inclusion of compensatory mechanisms in the form of placental hypertrophy, angiomatosis, sinusoidal transformation of the capillaries of terminal villi, thinning of the syncytiocapillary membrane associated with an increase in the content of von Willebrand factor in the villus syncytiotrophoblast, in aggregate, normalizes the exchange between maternal and fetal blood and creates certain prerequisites for the successful completion of pregnancy. However, thinning of the syncytiocapillary membrane increases the risk of rupture and direct contact of the internal media of the mother and the fetus.

Conclusions: Sedentary lifestyle of a pregnant woman leads to structural and functional changes in the placenta, which can be a serious prerequisite for the development of pathological abnormalities in the function of the "mother-placenta-fetus" system. To a certain extent, these changes are leveled due to compensatory processes in the placenta, the margin of efficacy of which needs further investigation.

KEY WORDS: placenta, sedentary lifestyle, pregnancy

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INTRODUCTION

The negative effect of physical inactivity on human health is a well-known and scientifically proven fact. A sedentary lifestyle and hypodynamia have become a kind of "portrait" of the inhabitants of the cities of Europe and, in particular, Ukraine. Among practicing obstetricians-gynecologists, there is still a conviction about the benefits of reducing physical activity during pregnancy, which supposedly reduces the risk of its premature termination. At the same time, scientific studies of recent years have proven the unambiguously negative effect of physical inactivity on general reproductive health and the course of the gestational process, condition of the fetus and newborn [1, 2, 3]. Experimental data on limiting the motor activity of pregnant animals are very indicative. In every fifth case, there was a resorption of the fetus and stillbirth, and in 35% of cases the offspring were found to be non-viable [4]. A prerequisite for pathological abnormalities during pregnancy, delivery and the postpartum period was endometrial hypoplasticity, combined with a decrease in contractile abilities of the myometrium [5]. Based on this, it is logical to assume the existence of deviations in the morphofunctional state of the placenta, the main provisional organ that plays a decisive role in the effective functioning of the mother-placenta-fetus system.

THE AIM

The aim of the was to study of the functional morphology of placenta in a sedentary lifestyle of a woman during pregnancy.

MATERIALS AND METHODS

Twenty placentas obtained as a result of deliveries at term were studied. Inclusion criteria: age 20–40 years; permanent residence in the city; the absence of clinically significant risk factors for obstetric pathology and concomitant somatic pathology requiring follow-up and treatment by appropriate specialists; no professional sports activities.

According to the WHO recommendations, physical activity of medium intensity, which includes walking at a medium or fast pace, for at least 150 minutes per week (about 20 minutes per day) should be considered normal

Table 1. Gestational age, mass-height and placentometric indicators in comparison groups

Indicators	"HD" group ($\overline{X} \pm S\overline{x}$)	"C" group ($\overline{X} \pm S\overline{x}$)
Gestation period, weeks	38.7 ± 0.4	39.8 ± 0.3
Average weight of placenta, g	633.3 ± 55.8	620.8 ± 44.0
Placental-fetal index	0.185 ± 0.011	0.173 ± 0.061
Weight of newborns, kg	3.50 ± 0.17	3.51 ± 0.15
Height of newborns, m	0.53 ± 0.01	0.53 ± 0.01
Height-weight index, kg/m^2	12.16 ± 0.73	12.28 ± 0.52

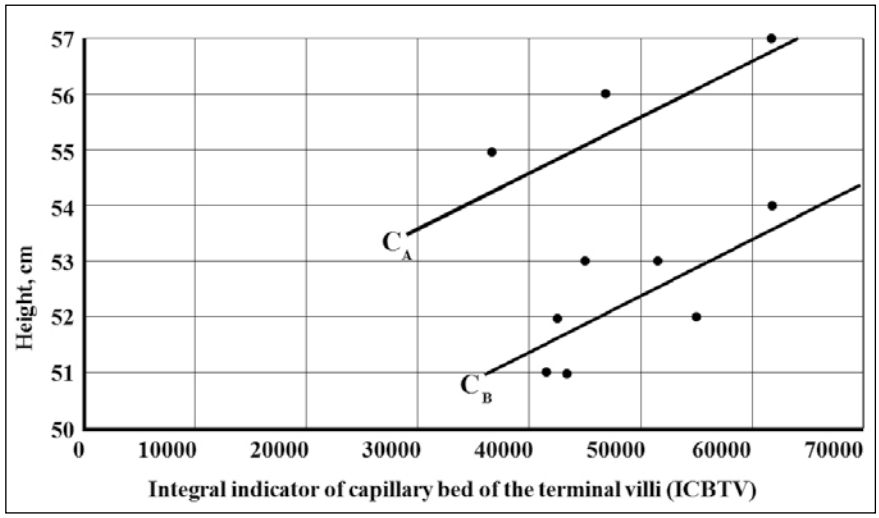

Fig. 1. Relation between the height of newborns and the integral indicator of the capillary bed of the terminal villi of placenta in the control group.

physical activity for this age group. In this case, the training session should be divided into time periods lasting at least 10 minutes [6, 7].

Women included in the study were offered a questionnaire that included 28 questions of self-assessment of the level of physical activity in everyday life using the multiple choice answer scheme. An objective assessment of the degree of motor activity of women was carried out by comparing the results in the questionnaire and the data of the OMRON Walking Style One 2.0 pedometer (Japan) that every woman wore for 10 days, followed by calculating the average distance (number of steps) traveled per day and duration of episodes of continuous physical exercise.

As a result, all cases were divided into the following observation groups:

– "HD" ("hypodynamia") – patients with a low level of physical activity, the total duration of episodes of physical activity (walking) for which did not exceed 10 minutes per day, and the distance traveled was less than 2000 steps per day (10 individuals);

– "C" – control group composed of women with a fairly high level of physical activity, the criteria of which were consistent with WHO recommendations (10 individuals).

The gestational age at the time of labor, the weight, height and height-weight index of the newborns (Quetelet index), the weight and size of the placenta, as well as the placental-fetal index were taken into account.

The placenta tissue obtained in the middle part of its radius was fixed in 10% neutral formalin. Paraffin sections were stained with hematoxylin-eosin, picro-fuchsin according to Van Gieson, gallocyanin-chrome alum according to Einarson for total nucleic acids, and periodic acid Schiff reaction was performed.

To determine the von Willebrand factor in the cytoplasm of endotheliocytes and syncytiotrophoblast, an immunohistochemical study was performed using antibodies from Prime-BioMed (Russian Federation). Morphometric studies were carried out on computer images of placental micropreparations using an Axiostar-plus microscope from Zeiss (Germany) with a Progress-C10+ camera using Video Test-3 software (Russian Federation). The number of terminal villi and the total number of capillaries in them within the photograph area were calculated, the thickness of the syncytiocapillary membranes and the optical density of the von Willebrand-positive cytoplasm of the syncytiotrophoblast of the villi were measured.

Statistical analysis of normally distributed data was carried out by parametric methods. Statistical hypotheses were tested using the t factor. Conclusions regarding statistical hypotheses were generated at a significance level of $p < 0.05$.

RESULTS AND DISCUSSION

The average gestational age at the end of pregnancy was slightly longer in the control group than in the "HD" group, despite the fact that delivery was at term in all cases. At

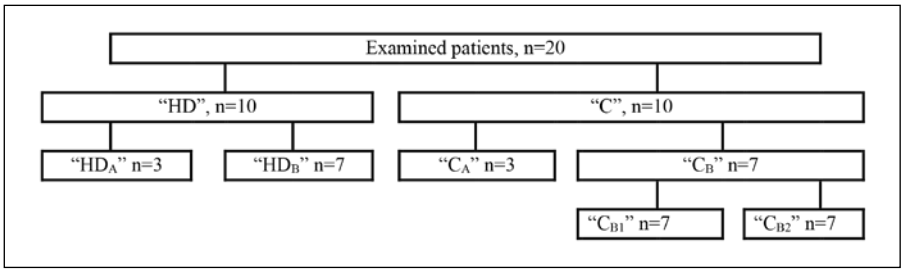

Fig. 2. Overall study design.

the same time, placentometric and weight-height indices did not significantly differ between the observation groups (Table 1).

The absence of a significant difference in the indicators we have obtained may be due to the fact that under the actual conditions of clinical observation, in addition to hypodynamia, there are many other external and internal factors that affect the placenta, which can not be taken into account, which may include diseases incurred during pregnancy, nutritional peculiarities, environmental hazards, etc. At the same time, favorable perinatal outcomes, despite the impact of alterative factors, are determined by the compensatory resources of placenta.

The results of numerous studies indicate an inevitable disturbance of blood supply to peripheral tissues associated with hypodynamia under both clinical and experimental conditions, based on which one should expect the presence of such disorders in the placenta [8, 9, 10]. To assess the degree of development of the capillary bed of terminal villi, we used an integral indicator, calculated as the product of the average number of capillaries of the terminal villi in a still frame (x100) and the mass of placenta: "Indicator of capillary bed of the terminal villi" (ICBTV). [11]. Comparison of the height of newborns and ICBTV made it possible to distinguish two subgroups in the "C" group: "C_A" and "C_B", in which a positive relation between a newborn's height and the placenta ICBTV value was observed, but at a different level (Fig. 1).

In the "C_A" subgroup, the newborns were taller (55–57 cm), the placentas turned out to be larger, and the placental tissue was mature histologically, there was stromal sclerosis of both large and terminal villi, intervillous fibrinoid was often present. The course of the gestational period in these women was complicated by anemia of the first degree. Placental hypertrophy with the phenomena of capillary hyperplasia of terminal villi (angiomatosis) concomitant with sclerotic processes and the formation of intervillous fibrinoid should obviously be considered as manifestations of adaptive processes associated with the indicated concomitant pathology, which in turn led to some acceleration of fetal development.

In the "C" group, the "C_B" subgroup was also distinguished (see Fig. 1), in which, on the basis of the results of evaluating the weight-height indicators and calculating the ICBTV values of placentas, two subgroups were distinguished: "C_{B-1}" and "C_{B-2} "(Fig. 2). The gestational process in women of the C_{B-1} subgroup proceeded without any complications. The newborns had a height of 52–54 cm, the weight of the placenta was about 600 g. Histological signs of placental damage in the form of sclerosis of the stroma of the villi, the formation of fibrinoid in the intervillous space were minimally presented, which allowed to consider these cases as "pure" control with physiological course of pregnancy (Fig. 3).

In the "C_{B-2}" subgroup, the course of pregnancy was complicated by mild anemia; newborns had a height of about 51 cm, the placenta weight was in the range of 450-550 g. Histologically, pronounced sclerosis of the villi and accumulation of fibrinoid took place. In these cases, normalization of the placenta capillarization occurred in different ways: due to placental hypertrophy, due to hyperplasia and an increase in the density of terminal villi, or due to their angiomatosis. However, of all the cases presented in the control group, the body length of the newborns in this subgroup turned out to be the smallest, which reflects the minimum severity of proliferative processes in them.

In all placentas of women with a low-active lifestyle ("HD" group), indisputable signs of damage to the placental tissue were revealed histologically: large and numerous intervillous foci of fibrinoid, many terminal villi replaced by fibrinoid; severe pericapillary sclerosis in functioning villi (Fig. 4).

An analysis of the relationship between the body length of newborns and placenta ICBTV allowed us to distinguish two subgroups in the "HD" group: "HD_A" and "HD_B" (see Fig. 3; Fig. 5).

In the placentas of "HD_A" subgroup, which had the largest mass (about 800 g), concomitant with pronounced sclerosis of placental villi and accumulation of fibrinoid, ICBTV varied within normal limits, and newborns had maximum height (55-60 cm), forming a positive relationship between ICBTV and newborn height. In "HD_B" subgroup, a similar relationship was found at a lower level: the placenta mass was 500–700 g with the height of newborns 50–54 cm. Histologically, there was even more pronounced sclerosis of terminal villi and accumulation of fibrinoid. In only one case, the placenta weight was minimal with the absence of angiomatosis of terminal villi, which apparently directly affected the severity of proliferative processes in the fetal tissues, and therefore its height (47 cm).

Thus, we can assume that the effect of alterative factors insignificant in intensity ("HD_A") leads to the development of compensatory processes in the placental tissue in the form of hypertrophy, hyperplasia, and angiomatosis of terminal villi, which is clinically manifested in intrauter-

Fig. 3. Placental villus of a woman from "C" group. Antigen-positive linear sites in syncytia. Immunohistochemical reaction to von Willebrand factor. Magnification x1000.

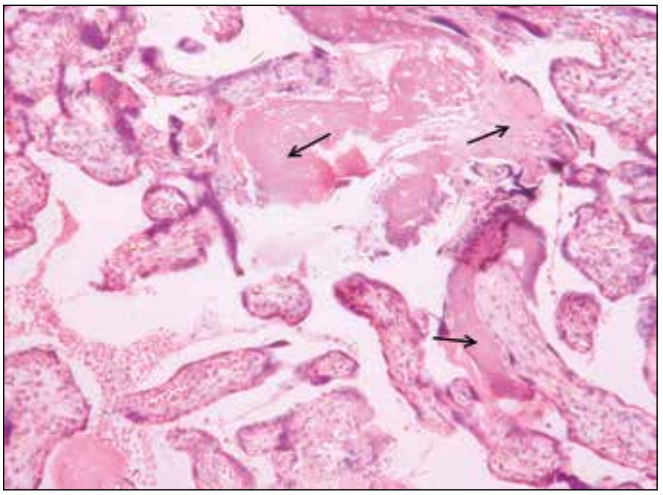

Fig. 4. Placenta of a woman from "HD" group. Space-occupying masses of fibrinoid are seen in the intervillous space. Hematoxylin and eosin staining. Magnification x100.

ine acceleration (tallness) of newborns. Large reserves of the compensatory potential of placenta when exposed to several or more intense damaging factors are confirmed by the constant value of ICBTV, despite the greater severity of signs of "aging", sclerosis in the placenta ("HD_B").

The average height of newborns, at the same time, corresponds to that in the physiological course of pregnancy (control), although it is much less than in the subgroup "HD_A". It is logical to assume that in order to compensate for the expressed alternative effects that lead to sclerosis of the stroma in the villi secondary to a sedentary lifestyle of a pregnant woman, a certain additional compensatory mechanism should be initiated in the placenta, which allows stabilizing the function of the fetal-placental complex.

As is known, the exchange between the mother and the fetus in the last weeks of gestation occurs in a diffuse manner through syncytiocapillary membranes forming in the terminal villi of the placenta in the process of shifting the syncytium nuclei to one focus with the formation of the syncytial nodule. The syncytiocapillary membrane consists of the following layers: syncytium cytoplasm, syncytium basal membrane, villus stroma, capillary basal membrane with fetal blood, capillary endothelium. At the end of gestation period, the thickness of the syncytiocapillary membrane reaches 3-5 microns. [12]. Obviously, thinning of the syncytiocapillary membrane leads to an intensification of exchange between the mother and the fetus in the placenta.

We measured the syncytiocapillary membrane thickness. It turned out that the thickness of this most important structural part of the placenta of women in the control group was significantly less than in the case of a sedentary lifestyle during the gestation period (Table 2). The thickness range of the syncytiocapillary membrane in the placenta of the control group was 2.07–4.92 μm, and the same in "HD" group was 1.13–3.59 μm. In the latter case, terminal villi in which the capillary protrudes beyond the rounded contour of its cross section are often encountered. In addition, syncytial nodules are generally larger than in the control, often with karyopicotic nuclei.

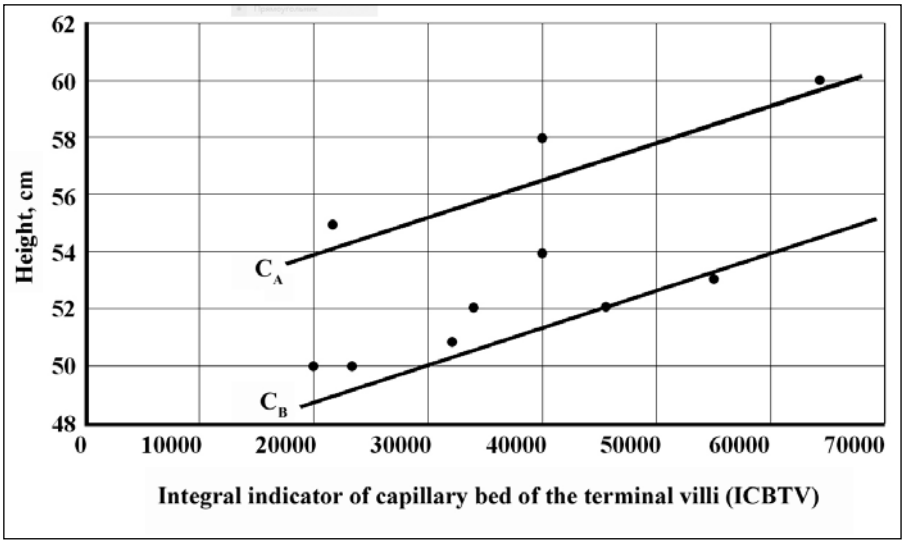

Fig. 5. The relationship between the integral indicator of the capillary bed of terminal villi of the placenta and the height of newborns in the "HD" group.

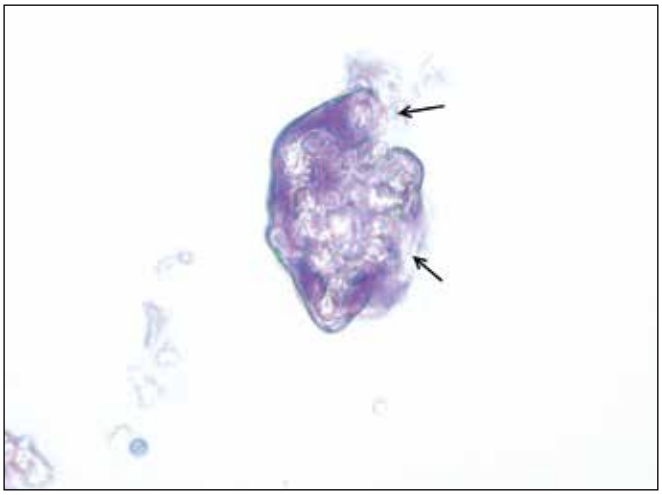

Fig. 6. A placental villus of a woman from "HD" group. There are two sites of destruction of the syncytiocapillary membrane with open mutual contact of the fetal and maternal blood. Immunohistochemical reaction of von Willebrand factor. Magnification x1000.

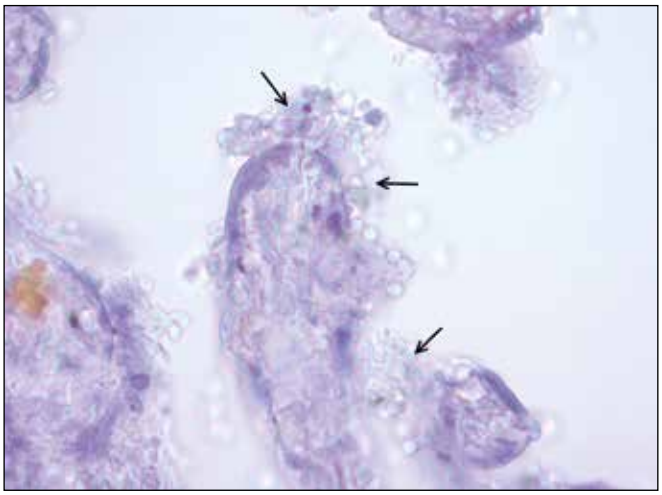

Fig. 7. A placental villus of a woman from "HD" group. Syncytium is lost on a large portion of the surface of the villus. The latter is blocked by fresh blood clots. Immunohistochemical reaction of von Willebrand factor. Magnification x1000.

The fact that the syncytiocapillary membranes are thinning can explain the nature of the ruptures of the syncytiocapillary membrane that are often observed in the placentas of "HD" group with the formation of a pattern of fetal blood "explosion" (Fig. 6). Obviously, this is a consequence of the compensatory thinning of the syncytiocapillary membrane, which occurs to normalize the exchange between the mother and the fetus in the placenta, often leading to the above-described acceleration of fetal growth.

The results of our immunohistochemical study of the placenta using antibodies to von Willebrand factor are noteworthy. This blood plasma glycoprotein, which is formed in the Weibel-Palade bodies of endothelium cells, assures platelet attachment to the damaged vessel by binding to other proteins, primarily coagulation factor VIII [13]. It was found that the endothelium of the capillaries of the placental terminal villi is practically not preserved, which is apparently due to the development of severe hypoxia during transection of the umbilical cord and separation of the placenta from the uterus. However, in the vessels of large villi, partial preservation of the endothelium with aggregation of erythrocytes on the basal membrane in the areas of its absence takes place. Synthesis of von Willebrand factor occurs not only in the cytoplasm of endotheliocytes, but also in the syncytial cover of the villi, which plays a huge role in preventing the mixing of maternal and fetal blood. When s syncytium site on the surface of a villus dies, fibrin begins to be deposited immediately (under the influence of von Willebrand factor), blocking the syncytiocapillary membrane. Antigen-positive substances are located linearly in the outer layer of syncytiocapillary membranes (Fig. 7).

Measurement of optical density of antigen-positive, i.e. labeled portions of the syncytiocapillary membranes revealed its increase in placentas of the "HD" group versus the control (see Table 2). An increase in the content of von Willebrand factor in the thinned syncytiocapillary membranes of the terminal villi of the placenta can be regarded as an adaptation mechanism that prevents direct contact of the internal media of the mother and the fetus.

CONCLUSIONS

1. In placentas of women with a sedentary lifestyle, there is an increase in the degree of formation of intervillous fibrinoid, fibrinoid substitution, and villous sclerosis, which leads to the "shutdown" of villi and, consequently, to a decrease in the normal functioning of the fetoplacental complex. Differences in mean somatometric

Table 2. The thickness of the syncytiocapillary membranes of the terminal villi and the optical density of the antigen-positive sites of syncytium during immunohistochemical reaction of von Willebrand factor

Group	Thickness of the syncytiocapillary membranes of the terminal villi, μm ($\overline{X} \pm S\bar{x}$)	Optical density of the antigen-positive sites of syncytium (conventional units of optical density) ($\overline{X} \pm S\bar{x}$)
C	3.55 ± 0.16	0.153 ± 0.009
HD	2.4 ± 0.12**	0.198 ± 0.004*

Remarks:
* – $p<0.01$ versus the control;
** – $p<0.001$ versus the control.

indices of newborns in comparison groups, however, are not statistically significant.
2. Hypertrophy of placenta with an increase in its weight and volume, villus hyperplasia, terminal villi angiomatosis, sinusoidal transformation of terminal villi capillaries reflect the huge compensatory potential of the placenta, and, according to morphometric studies, these compensatory mechanisms are equally used in both groups studied.
3. Thinning of the syncytiocapillary membrane was revealed in terminal villi of the placenta of women with a sedentary lifestyle, associated with an increase in the content of von Willebrand factor in the syncytiotrophoblast of the villi, which should be interpreted as triggering of another compensatory mechanism that normalizes the exchange between maternal and fetal blood with concomitant increased risk of syncytiocapillary membrane rupture and direct contact of the internal media of the mother and fetus.

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Conflict of interest:

The Authors declare no conflict of interest.

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