

expression characterizing to therapy and prognosis of the disease evidently intensify the tendency to individualization of planning and performing of adjuvant therapy.

## **Pregnancy and perinatal outcomes in women with a history of ovarian hypofunction**

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**Summary:** 95 pregnant women with a history of ovarian hypofunction (study group) and 30 with normal menstrual cycle (control group) were prospectively examined. Pregnancy had complicated by threatened interruption of placental insufficiency and preeclampsia in the main group. 6.1% of the children were born in asphyxia. The placental growth factor (PIGF), its free receptor (VEGFR-1) and value PIGF/VEGFR-1 were examined in the blood serum of pregnant women, and their levels were lower in the study group compared to the control ( $p < 0.05$ ). It is concluded that the possibility of their value in placental angiogenesis and development of primary placental insufficiency in 8.4% of pregnant women. The content of  $\beta$ -human chorionic gonadotropin ( $\beta$ -HCG), progesterone (PG) and  $\alpha$ -fetoprotein ( $\alpha$ -FP) is lower in the blood of pregnant women in the basic group than in the control, which is typical of placental insufficiency.

**Keywords:** pregnancy, the placenta, placental growth factor, a newborn.

Worldwide the frequency of gynecological diseases among adolescent girls is increasing [1, 14]. Violations of becoming the menstrual function reaches 61 % [11, 15]. The ovarian hypofunction has a value in this disease because of the immaturity of neuroendocrine regulation. Clinical manifestations of ovarian hypofunction are delayed puberty and oligomenorrhea. Violations at the level of the hypothalamic-pituitary axis is one of the causes of endometrial hyperplasi and of disorders of the blood supply to the uterus and ovaries [5, 8, 16]. Women with ovarian hypofunction in the period of menstruation increases the frequency of infertility, miscarriage [9, 13]. In 52.6% of pregnant women formed placental insufficiency due to violation of the quantitative and qualitative relationships between ovarian steroid hormones and their receptors in the endometrium [1, 12].

The ratio of blood flow in the vessels of the uterus affects the willingness of the endometrium for implantation. [8]. Endometrial vascularization associated with the action of sex steroid hormones. Estrogens stimulate the expression of vasculoendotelial growth factors (VEGF) in the endometrium, which is important in the formation of placental bed. [17] Placental insufficiency underlies the development of obstetric complications and perinatal outcomes [6, 10]. The purpose of the study. To study the course of pregnancy and perinatal outcomes in women with a history of ovarian hypofunction who received treatment in adolescence and the reproductive years.

### **Materials and methods.**

125 pregnant women involved in a prospective clinical study, 95 of them had a history of ovarian hypofunction (study group) and 30 - normal menstrual cycle (control group). Newborns of surveyed mothers ( $n = 96$ ) and ( $n = 31$ ) were the respective groups (in groups is one twins). Pregnant women age is  $26,3 \pm 0,9$  and  $24,7 \pm 0,5$  years ( $p > 0.05$ ). Age of menarche is  $15,4 \pm 1,1$  and  $12,6 \pm 0,9$  years ( $p < 0.05$ ) in groups, respectively. 65 pregnant women in the study group had a history of delayed puberty, which characterized by late onset of menstruation and 30 women had not a regular menstrual cycle. All patients were treated in adolescence and childbearing age and examined by us in the planning of this pregnancy. The normal function of the pituitary

gonadotrophin and hypovarianism were identified in those women as a result of hormonal studies. [2].

Exclusion criteria were overweight, obesity, hyperandrogenism, severe physical illness.

Clinical, laboratory and functional studies were used in the work. Venous placental growth factor(PIGF) and its receptor(VEGFR-1) were investigated by ELISA in the serum of venous blood 10-14 and 16-20 weeks, and  $\alpha$ -OP,  $\beta$ -hCG and progesterone at 11-12 weeks of pregnancy. Hemodynamics in the uterine arteries and umbilical artery were examined by ultrasound machine «LOGIQ 400 pro» with doppler prefixed at 22-24 and 32-34 weeks of pregnancy. Mathematical processing of the data was carried out using Microsoft Office Excel 2007 and statistical software package «Statistica 6.0». Differences were evaluated as statistically significant at  $p < 0.05$ .

### Results and discussion.

In the analysis of pregnancy complications of pregnancy was diagnosed 1.5 times more frequently in patients with ovarian hypofunction (Table 1) as compared to pregnant control group ( $p < 0.001$ ). The structure of complication rates were follow: a threatening miscarriage (8.4%), threatening preterm delivery (20.0%), placental insufficiency (50.5%), preeclampsia (28.4%). Primary placental insufficiency (8.4%) diagnosed only in the main group of pregnant women.

97 babies were born in the study group, including 5 prematurity (4 of twins and one child in the mother with preeclampsia). 6 (61%) infants were born in the average severity of asphyxia. The average birth weight was  $3315 \pm 19,8 \pm 17,2$  and 3441 grams ( $p < 0.001$ ) in the groups, respectively. In 22.1% of the newborns of the main group identified the disease in the early neonatal period. Structure of neonatal diseases: cerebral ischemia 12.6%, respiratory distress syndrome 4.2% and malnutrition 5.3%. In the control group all the children were healthy.

**Table 1.**

**The frequency and structure of complications of pregnancy in the target groups**

Group	Nosological form												Only	
	Threat of termination				Placental insufficiency				Preeclampsia		Anemia			
	up to 22 weeks		22-37 weeks		primary		chronic							
	abs	%	abs	%	abs	%	abs	%	abs	%	abs	%		
Summary (n=95)	8	8,4	19	20,0	8	8,4	48	50,5	27	28,4	26	27,3	136	143,2
The control (n=30)	3	10,0	1	3,3	-	-	6	20,0	2	6,6	3	10,0	15	50,0

Note: \* -  $p < 0,05$ ; □ □ -  $p < 0,01$ ; □ □ □ -  $p < 0,001$ .

□ - level of statistical significance of the differences between the main group and the control group.

Due to the high incidence of complications of pregnancy and neonatal disease in women with a history of ovarian hypofunction, we studied placental growth factors regulating angiogenesis in the placenta (Table 2). PIGF grew up in 2.8 times ( $p < 0.05$ ) with increasing gestational age of patients in the study group, in the control group - in 2.3 times ( $p < 0.05$ ). PIGF was lower in the study group compared with the control group in studied terms of pregnancy. At a lower content of PIGF in women with a history of ovarian hypofunction content of its receptor VEGFR-1 was 1.5 times higher than in the control group. In the main group containing between PIGF and VEGFR-1 is set at 10-14 weeks depending inverse measure ( $r = -0,21$ ), it is stronger at 16-20 weeks ( $r = -0,35$ ;  $p < 0.05$ ). In pregnant of control group depending measure is stronger compared with the basic group ( $r = -0,48$  and  $r = -0,52$ ;  $p < 0.05$ ). Increasing of free VEGFR-1 in serum of pregnant in basic group can be explained by the formation of small complexes PIGF-VEGFR-1 due to the reduction of PIGF.

**Table 2.****Contents of placenta growth factor and its receptor in serum of pregnant surveyed groups**

Group	PlGF pg/ ml		VEGFR-1 ng/ml	
	10-14 weeks	16-20 weeks	10-14 weeks	16-20 weeks
Summary (n=20)	26,4±6,3	74,4±11,4	1,8±0,4	1,4±0,3
The control (n=10)	49,8±13,9	113,1±23,5	1,3±0,4	0,9±0,3

We obtained the following results in the study of the endocrine function of the placenta of pregnant test groups (Table 3). The content of  $\beta$ -hCG for pregnant women with a history of ovarian hypofunction was 2 times lower compared with the control group ( $p < 0.001$ ). A similar pattern is set to the content of PG ( $p < 0.05$ ). Reduction of the endocrine function of the placenta in pregnant of the main group is one of the primary criteria for placental insufficiency.

It is known that the fetus experiences a state of hypoxia in placental insufficiency. The spasm of peripheral vessels and blood redistribution occurs in the fetus under these conditions. Kidney and liver, which is produced by  $\alpha$ -FP, are suffering [7]. In our studies, the content of  $\alpha$ -FP in the serum of pregnant of the main group is  $34,4 \pm 3,5$  ng / ml, control - is  $46,0 \pm 7,4$  ng / ml ( $p < 0.05$ ). This shows a decline albuminiferous liver function in the fetus that may have a hypoxic origin.

In pregnant women with a history of ovarian hypofunction IR in the uterine arteries is higher compared with the control group ( $p < 0.001$ ) (Table 4). Reduced uterine hemodynamics occurs due to lack or incomplete trophoblast invasion in the spiral arteries. While reducing uteroplacental blood flow in the umbilical artery the IR is higher in the main group compared with the control group ( $p < 0,001$ ). The curve of the blood flow velocity in the umbilical arteries characterized by the reduction of diastolic blood flow velocity, indicating a significant increase in peripheral vascular resistance of the fetal part of the placenta.

**Table 3.****The content of  $\alpha$ -fetoprotein,  $\beta$ -subunit of chorionic gonadotropin and progesterone in serum of pregnant surveyed groups**

Group	$\alpha$ -FP ng/ ml	$\beta$ - hCG mEg/ ml	PG nmol/l
Summary(n=95)	34,4±3,5 □	26344,4±2961,9 □ □ □	90,9±4,7 □
The control (n=30)	46,0±7,4	56399,0±13422,4	106,0±3,3

Note: \* -  $p < 0,05$ ; □ □ □ -  $p < 0,001$ .

□ -level of statistical significance of the differences between the main group and the control group.

**Table 4.****Indicators of resistance index in pregnant women surveyed groups 22-24 and 32-34 weeks**

Group	Resistance index (components units.)					
	22-24 weeks			32-34 weeks		
	uterine artery on the right	uterine artery on the left	umbilical artery	uterine artery on the right	uterine artery on the left	umbilical artery
Summary(n=95)	0,54±0,01 □ □ □	0,56±0,01 □ □ □	0,67±0,01 □ □ □	0,53±0,01 □ □ □	0,55±0,01 □ □ □	0,65±0,01 □ □ □
The control(n=30)	0,50±0,01	0,51±0,01	0,59±0,01	0,49±0,01	0,49±0,01	0,55±0,01

Note: □ □ □ -  $p < 0,001$ .

□ -level of statistical significance of the differences between the main group and the control group.

### **Conclusions:**

1. The threat of miscarriage, preeclampsia, placental insufficiency are the most frequent complication in patients with a history of ovarian hypofunction. Primary placental insufficiency was diagnosed in 8.4% of pregnant women.

2. In 22,1% of infants born to mothers with a history of ovarian hypofunction, diagnosed the following diseases: ischemic brain hypoxic genesis, respiratory distress syndrome, malnutrition.

3. Reduction of PIGF, increasing VEGFR-1 and a lower ratio of PIGF/VEGFR-1 in pregnant women with a history of ovarian hypofunction compared with pregnant women who have a normal menstrual cycle, may be responsible for violations of angiogenesis in the placenta, placental insufficiency and fetal hypoxia by clinical data, reducing the content of  $\beta$ -CG, SG,  $\alpha$ -PT serum and increasing of IR in the uterine arteries and umbilical artery.

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## The role of citomegalovirus in children with acute respiratory viral infections

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Over the past 30 years there were revealed more than 30 kinds of infectious diseases, among which a special place occupies cytomegalovirus (CMV), which is caused by a virus belonging to the family of herpes viruses. It is known that the source of infection - a person infected with or affected by the acute form. In most cases cytomegalovirus proceeds latently, but becomes dangerous during pregnancy, perinatal period, in young children, as well as at immunodeficiency. After primary infection, the virus is not derived from the host and circulates there in a lifetime. Up to 3% of infants are born infected with cytomegalovirus (CMV) and 10% of the cases in the future suffer from its complications - lesions of the central nervous system - CNS, gastrointestinal tract, eye, lung, heart, organs of hematopoiesis. Unfortunately, there is rarely diagnosed CMV infection in pregnant women and in children at birth. Therefore, the primary implementation of acute respiratory viral infections (ARVI) in children is first detected long low-grade fever, the occurrence of lymphadenopathy and mononucleosis syndrome that causes a doctor to examine the child to herpesviruses and in particular CMV. In the past three years there were fulfilled clinical and laboratory studies of treatment and prevention measures and study the effectiveness of various therapeutic approaches to herpesvirus infections (CMV) in children in the Amur Regional Hospital of Infectious Diseases in Blagoveshchensk.

**Keywords:** cytomegalovirus, CMV infection, immune globulin, acute respiratory viral infections, infectious diseases

### Materials and Methods

We observed 22 children aged from 6 months up to three years, admitted with a diagnosis of ARVI. In this group of patients, DNA to CMV was found in 10 children, in 12 children - to the ARVI virus and CMV. The etiological diagnosis was established due to on the results of research material from children (nasal swab on ARVI viruses) for CMV - identifying cells in urine, saliva, blood using polymerase chain reaction (PCR) and specific antibodies by enzyme-linked immunosorbent assay (ELISA). Table 1 presents the results of a survey of children for markers of CMV infection.

Table 1. The results of a survey of children markers of CMV infection

Materials research	The number of examined	Markers of CMV detection	
		Abs.	%
IgM – anti - CMV	14	1	7,1
IgG – anti - CMV	22	14	63,6
IgM+IgG – anti - CMV	22	14	63,6
Avidity of antibodies (high avidity)	14	9	64,3
Avidity of antibodies (low avidity)	14	8	57
PCR blood	7	1	14,3
PCR saliva	14	9	64,3
PCR urine	6	2	33,3

Detection in children of anti - IgM - CMV and anti - IgG - CMV simultaneously, and identification of CMV antigen in blood and urine indicate that there is a form of acute or reactivated