ORIGINAL ARTICLE

CONTENTS

The burdened medical history of the mothers-in-partum – risks for the newborn

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ABSTRACT

Aim: To improve early diagnosis in the mothers-in-partum, with a burdened of medical case history, taking into account the pathological pattern «mother-newborn» analysis

Materials and Methods: Two groups of mothers-in-partum (n=109) with burdened anamnesis were analyzed, in comparison with mothers of children with control group date(n=31).

Results: As for the course of pregnancy, there was a predominance of values of chronic Fetoplacental insuffieciency data (33,91±2,16 vs. 12,92±2,36%, p<0,001), Preeclampsia (38,54±1,67 vs. 22,67±2,48 %, p<0,001) in comparation with control group date. Regarding the course of labour, deliveries by Cesarean section were the most frequent among mothers in the first group in comparison with the data of the control group (55,03±3,28 vs. 45,21±2,48%, p<0,01) along with early discharge of amniotic fluid (44,95±1,39 vs. 38,70±1,46%, p<0,01). Suppression of IL-10 level, is observed at high levels of Anti-Toxoplasma-IgG, as evidenced by the negative correlation between them (r=-0,27, p=0,004). However, Anti-HSV 1/2-IgG does not have a negative effect on the level of Neopterin in infants. The relationship between Anti-CMV-IgG and IL-1 (r=0,75, p<0,001) indicates the stimulation of the inflammatory process in premature infants and inhibition of IL-10 synthesis (r=-0,29, p=0,002).

Conclusions: A negative correlation between IL-10 level in infants and levels of Anti-Toxoplasma-IgG in mothers, similar relationship was detected regarding Anti-HSV 1/2-IgG on level of TNF-α. Anti-CMV-IgG and IL-1 correlation analysis detected the stimulation of inflammatory process in premature infants and inhibition of IL-10 synthesis.

KEY WORDS: mothers-in-partum, burdened medical history, risk factors, Caesarean section, intrauterine infections, newborns

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INTRODUCTION

Diagnosis of intrauterine infections (IUI), given the non-specificity of clinical manifestations, is possible taking into account risk factors in a pregnant woman, data from functional studies, as well as a general blood test, which allows us to assume the presence of an inflammatory process, even in the absence of clinical manifestations. Examination of 65 pregnant women at 32-36 weeks of gestation and 62 newborns with IUI (32 full-term and 30 premature) was carried out [1]. The diagnosis of IUI was verified by peripheral blood tests for the presence of antigens and antibodies to the causative agents of streptococcal, CMV, HSV, Candidal, Chlamydial, Mycoplasmal, and Ureaplasmal infections.

A CBC test in pregnant women showed a decrease in the concentration of hemoglobin by 21%, erythrocytes by 38%. Leukocytosis was observed with a shift of the leukocyte formula to the left by 18%. In severe infections, the leukocyte formula changed due to an increase in the number of segmented neutrophils and the appearance of more young forms. ESR levels were elevated in 17% of cases. However, in 6% of cases, no changes were detected.

During a comprehensive clinical examination, 75% of newborns were diagnosed with intrauterine pneumonia, 14% with conjunctivitis, 6% with enterocolitis, and 3% with pyelonephritis. In other children in the early neonatal period, clinical manifestations of IUI were not detected.

In the general blood test, specific changes characteristic for infection were found in all children. An increase in the number of lymphocytes and segmented neutrophils was found in 56% of cases. At the same time, the number of leukocytes did not exceed the normal level in 25% of cases. The most pronounced changes in the general blood analysis were noted in streptococcal infection, as well as in its combination with CMV. No significant differences were found in ureaplasma infection.

A significant increase in the concentration of Na ions (151.1±2.7 mmol/l) in blood serum and a tendency to increased concentration of Ca ions (2.9±0.01 mmol/l) were found in newborns with IUI. In contrast, there was a decrease in the concentration of K ions (2.4±0.05 mg-eq/l), which indicates the development of an imbalance in the serum electrolyte composition in children with IUI. In addition, with a very severe course of the disease with pronounced respiratory insufficiency, with colitic and hyperthermic syndrome, more pronounced hypernatremia with increasing hypokalemia appears. The ionic composition of blood plasma differed depending on the nosological form of BUI. Infectious pathology intensifies changes in the electrolyte balance, as it disrupts the transport of microelements at the cellular level [1].

The transfer of maternal IgG begins at approximately 13 weeks of pregnancy, at the beginning of the second trimester, and has long been recognized as a central component of the formation of fetal immunity against pathogens. Infectious diseases of the mother change the system of signals that form a complex network of interactions and, thus, can change the immunity of the fetus [2].

In case of viral infection, trophoblasts constitutively secrete antiviral IFNs, which limit the infection both autocrinely and paracrinely. The release of type III IFNs is a unique feature of trophoblasts, as IFNs are usually induced only in response to viral infection. As antiviral effectors of the interferon pathway, IFN-stimulated genes (ISGs) can exhibit potent cytotoxic and proinflammatory properties [3, 4]. In addition to IFNs, trophoblasts also secrete antiviral micro-RNAs in the placental exosome, which provide antiviral protection in non-placental cells and can be isolated from the blood serum of pregnant women [5, 6].

Thus, the problem of diagnostic possibilities of intrauterine infections of newborns remains relevant due to the lack of a specific clinical presentation in the early stages of the pathological process and the low diagnostic capacity of the available examination methods. At the same time, the use of only clinical signs causes numerous diagnostic errors, which requires the mandatory use of laboratory, microbiological, morphometric, and molecular genetic studies.

AIM

To improve early diagnosis in the mothers-in-partum, with a burdened of medical case history, predicting the consequences of intrauterine infections in neonates, taking into account the analysis of the pathological pattern «mother-newborn» for the development of optimized therapy.

MATERIALS AND METHODS

In order to find out the predictors of the development of the pathological pattern «mother-newborn», two groups of mothers-in-partum (n=109) who had laboratory-confirmed TORCH-infection (IgG above the level of reference values) were analyzed, in comparison with mothers of children with control group (n=31).

INCLUSION CRITERIA WERE

women in labor, premature birth, burdened medical history, identified TORCH infection (IgG above the level of reference values).

EXCLUSIONS

physiological childbirth, oncological and autoimmune diseases, laboratory detection of TORCH infection (IgM), human immunodeficiency virus (HIV), viral diseases (rubella, hepatitis, chicken pox), tetanus, syphilis, gonococcal infection, tuberculosis, malaria, intestinal infectious diseases , candidiasis, severe developmental disabilities, alcohol and drug use.

RESULTS

In order to identify and analyze patterns of pathology development in children, a detailed analysis of the somatic and gynecological status of mothers was carried out in comparison with the data of the control group. The accompanying pathology in the mothers of the studied contingent of infants is considered in the table (Table 1).

According to Table 1, only 13 (41,9%) mothers of the control group were observed without pathology. Attention is drawn to the highest prevalence of anemia during pregnancy (52(48, 4±5,2%) versus 3(9,6±2,1%) in pregnant women of the control group. A high level of extragenital pathology in women in childbirth was observed due to diseases of the urinary system (21(19,2±2,4%) and diseases of the digestive system (18 (16,5±2,9%)). During the study of the morbidity of the digestive system in pregnant women with identified TORCH infection, pathology of the hepatobiliary system, in particular non-alcoholic fatty liver dystrophy was found, along with upper digestive tract involvement. According to scientific studies, disruption of biochemical processes of the liver and pronounced reflux esophagitis indicate negative effects of TORCH infection on mothers and, potentially, on newborns [7, 8].

The highest reliable indicator (<0.001) was observed in the category of cases of inflammatory diseases of the genital organs of women in childbirth in the main group (60(55,2±3,1%) versus 2(6,4±1.3%) of the control group, p<0.001). There is also a high reliable indicator for the diagnosis of anemia (52(48, 4±5,2%)

Table 1. Somatic and gynecological status of mothers of the studied contingent of infants

Parameters	The studied group (n=109)	Control group (n=31)	P
Extragenital pathology			
Urinary system diseases	21(19,2±2,4%)	7(22,6±%)	>0,05
Digestive system diseases	18(16,5±2,9%)	4(12,9±%)	<0,05
Cardiovascular system diseases	5(4,6±1,7%)	1(3,2±%)	<0,05
Anemias	52(48,4±5,2%)	3(9,6±2,1%)	<0,002
Associated gynecological diaseases			
Significant perinatal infections	9(8,3±%)	0	
Polycystic ovaries	2(1,8±0,8%)	1(3,2±1,1%)	<0,001
Inflammatory diseases of the genital organs	60(55,2±3,1%)	2(6,4±1,3%)	<0,001
Without pathology	0	13(41,9±3,2%)	

Table 2. Reproductive anamnesis of the mothers of the studied contingent of infants

Parameters	N=109	N=31	P
Artificial termination of pregnancy	21(19,3±1,7%)	6(19,4±2,1%)	>0,05
Miscarriages	26(23,9±2,1%)	3(9,7±2,2%)	<0,001
Work under toxic conditions	4(3,7±%)	1(3,2±%)	>0.05
Total	51(46,9%)	10(32,3%)	

against the data of the control group (3(9,6±2,1%), p<0,002). Comparative characteristics of other extragenital nosologies were uninformative.

Reproductive history of mothers is analyzed in the following table (Table 2).

According to women's anamnesis, reproductive dysfunction was detected in 51 (46,9%) mothers of children from the first and 10 mothers (32,3%) from the control group. Significant differences were observed as for the number of miscarriages (26 (23,9±2,1%) vs. 3(9,7±2,2%), (p<0,001), which is confirmation of fetopathy, caused by TORCH infections in most cases.

The information about the course of pregnancy in mothers is important as well (Table 3, Fig. 1).

According to table 3 and fig. 1 there is a predominance of the values of CFPI data (33,91±2,16 vs. 12,92±2,36% in the control group, p<0,001), cases of preeclampsia (38,54±1,67 vs. 22,67±2,48 %, p<0,001) and threatenes miscarriage (16,54±2,91 vs. 9,21±1,27%, p<0,001). Determination of CFPI, threatened miscarriage and premature birth as the main manifestations of fetopathy due to IUI are observed in the studied newborns.

Data of the course of childbirth among the mothers of the studied groups of infants is reflected in the following table (Table 4).

Among the individual indicators (Table 4), deliveries by Cesarean section were the most frequent among mothers in the first group in comparison with the data of the control group (55,03±3,28 vs. 45,21±2,48%, p<0,01) along with early discharge of amniotic fluid (44,95±1,39 vs. 38,70±1,46%, p<0,01). Rapid childbirth, on the contrary, was more often observed in the mothers of the control group of infants (32,26±1,18 vs. 18,34±2,17, p<0,001).

The analysis of the data of mothers with identified TORCH infection, by number of pregnancies, is presented on Fig. 2.

According to the data of Fig. 2, among the contingent of mothers, the most frequently odbserved cases were of second (44%) and the less frequent - of third pregnancies (6%).

Information on the distribution of women by the number of births is presented on Fig. 3.

Levels of childbirth cases by their number: the highest level was recorded at the first - 48% and the second - 40% birth, the lowest - at the fourth birth (4%). Mothers underwent screening for TORCH infection, when serum was collected for the study in the first trimester of pregnancy (10,32±1,18 weeks of gestation).

For research and sampling, a group of pregnant mothers formed a contingent with Anti-TORCH IgG levels above the reference values (Table 5).

The value of the Anti-Toxoplasma-IgG level (100,67 ± 94,67 IU/ml), which exceeds the upper limit of reference values by more than 12 times, is particularly indicative. High levels (>200,0 IU/ml) were observed in 32 pregnant women. Anti-HSV 1/2-IgG levels also exceeded physiological ranges up to 8 times, Anti-CMV-IgG - up to 8 times.

Table 3. Characteristics of pregnancy in mothers of infants

Parameters	First group (n=109)		Control group (n=31)		The index of P
	Abs.	%	Abs.	%	
Chronic fetoplacental insufficiency (CFPI)	37	33,91±2,16	4	12,92±2,36	<0.001
Toxicosis	18	16,54±2,91	4	12,92±2,36	>0,05
Threatened miscarriage	18	33,91±2,91	3	9,21±1,27	<0.001
Preeclampsy	42	38,54±1,67	7	22,67±2,48	<0.001

Note. P – reliability between groups.

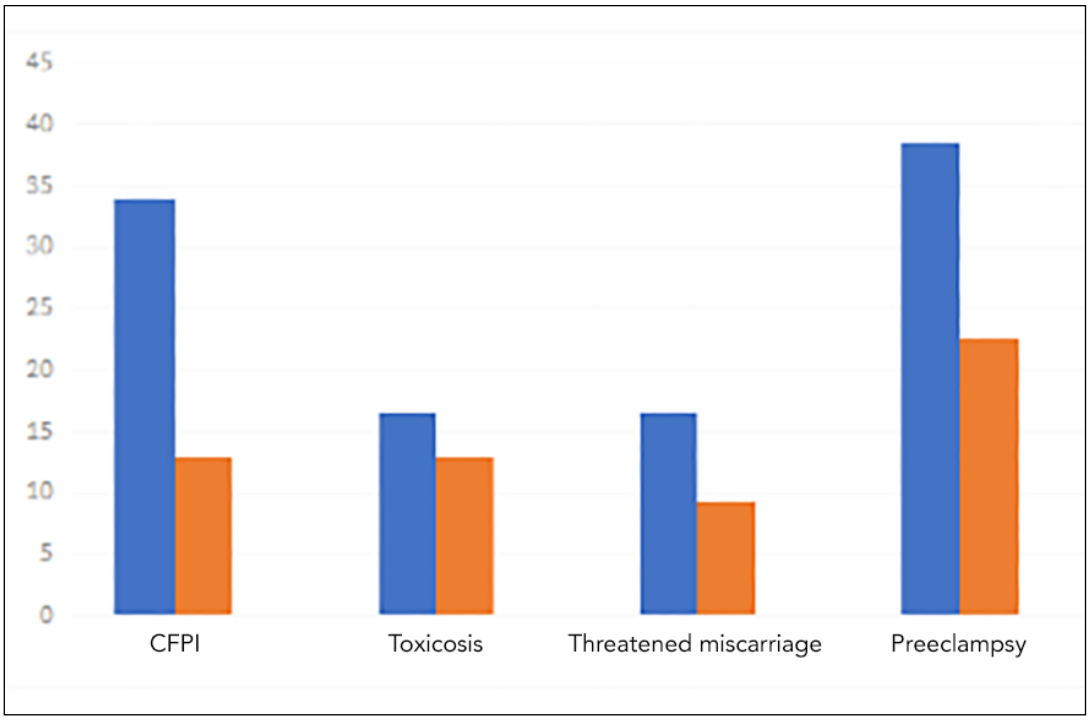

Fig. 1. The course of pregnancy in the mothers of the research groups.

To analyze and assess the risks of having children from mothers with TORCH infection, a correlation analysis of the relationships between the levels of TORCH antibodies in mothers and parameters of the inflammatory response in infants was conducted (Table 6).

Suppression of IL-10 level, as an anti-inflammatory factor in infants, is observed at high levels of Anti-Toxoplasma-IgG, as evidenced by the negative correlation between them (r=-0,27, p=0,004). The effect of Anti-HSV 1/2-IgG on the level of TNF-α has similar negative effects (r=-0,24, p=0,01). However, Anti-HSV 1/2-IgG does not have a negative effect on the level of neopterin in infants, on the contrary, it has a positive correlation (r=0,92, p<0,001), which indicates the absence of an effect on the inhibition of neopterin synthesis. The relationship between Anti-CMV-IgG and IL-1 (r=0,75, p<0,001) indicates the stimulation of the inflammatory process in premature infants and inhibition of IL-10 synthesis (r=-0,29, p=0,002).

The most indicative correlograms of the relationships between antibodies to HSV 1/2 IgG and neopterin and antibodies to CMV IgG and IL-1 are presented on Fig. 4, Fig. 5., respectively.

According to our data, chronic fetoplacental insufficiency (CPFPI) of mothers with a history of TORCH infections was observed in 37 (33,91±2,16%) women with an identified TORCH infection. The obtained data should be taken into account by neonatologists for more careful monitoring of newborns at risk of perinatal infections.

DISCUSSION

The fact that most of the diseases of pregnant women leading to IUI occur in a subclinical latent form with activation of the process in case of any homeostasis violation, can complicate the clinical diagnosis. At the same time, diagnosis based on clinical manifestations, without the involvement of specific microbiological

Table 4. Characteristics of childbirth in mothers of infants

Course of childbirth	First group (n=109)		Second group (n=31)		The index of P
	Abs.	%	Abs.	%	
Cesarean section	60	55,03±3,28	14	45,21±2,48	<0,01
Prolonged childbirth	29	26,60±2,17	7	22,58±1,37	>0,05
Rapid childbirth	20	18,34±2,17	10	32,26±1,18	<0.001
Stimulation of labor activity	49	44,95±2,31	14	45,16±2,48	>0.05
Early discharge of amniotic fluid	49	44,95±1,39	12	38,70±1,46	<0.01

Notes. P-reliability between groups

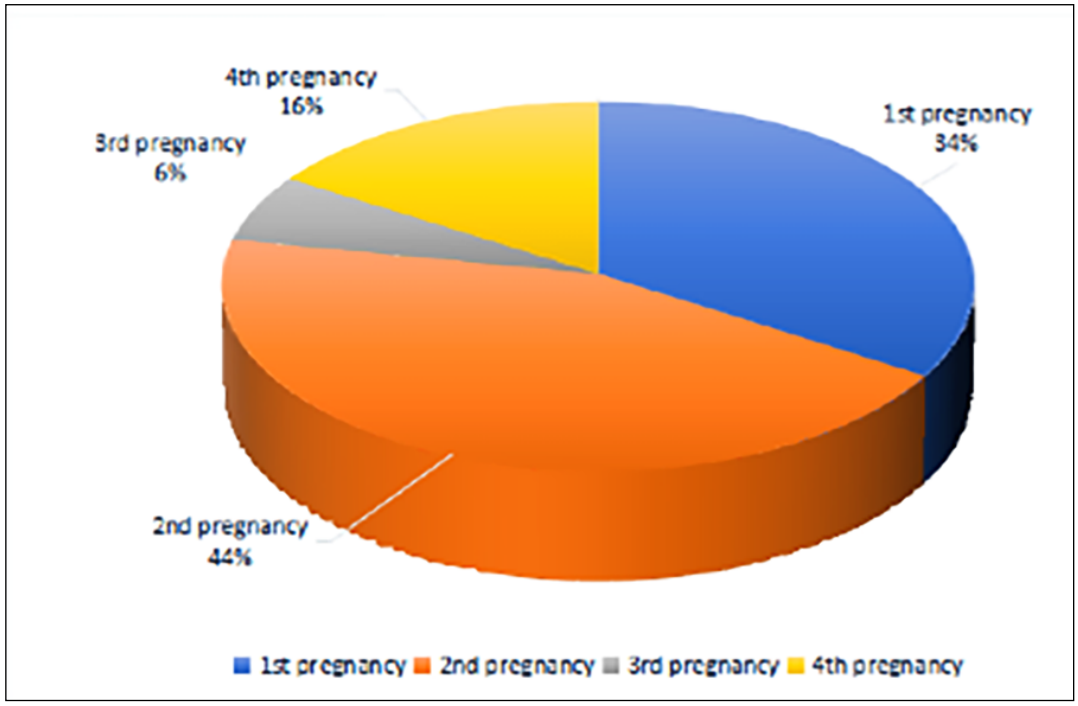

Fig. 2. Distribution of women by number of pregnancies.

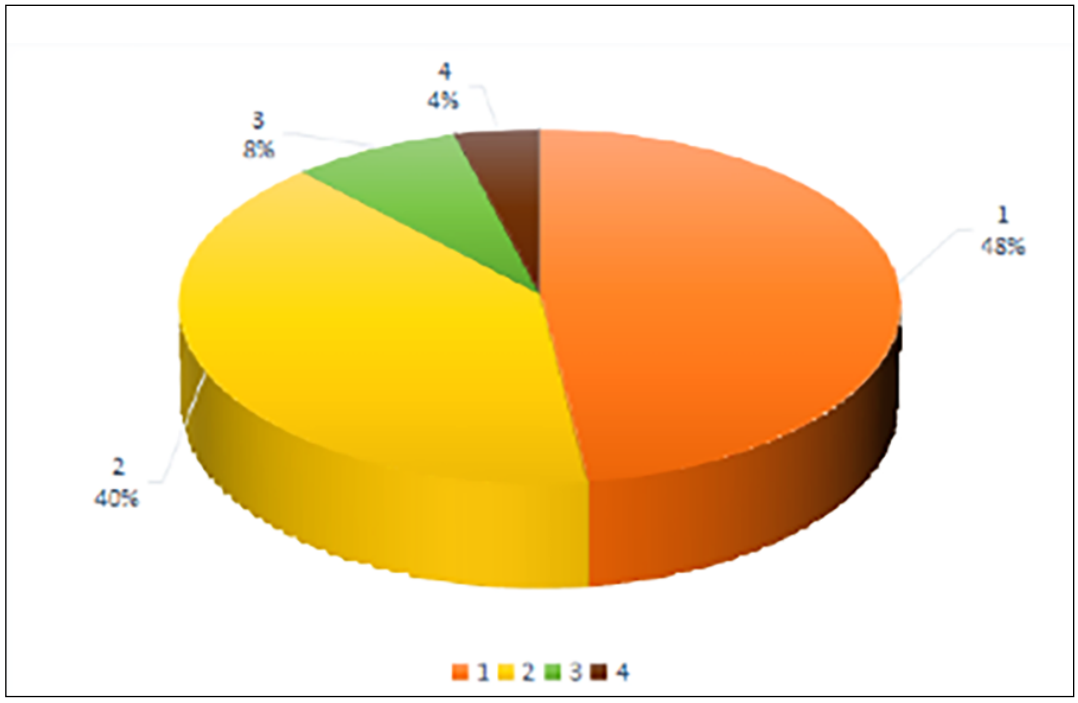

Fig.3. Distribution of women by number of deliveries (no.; %).

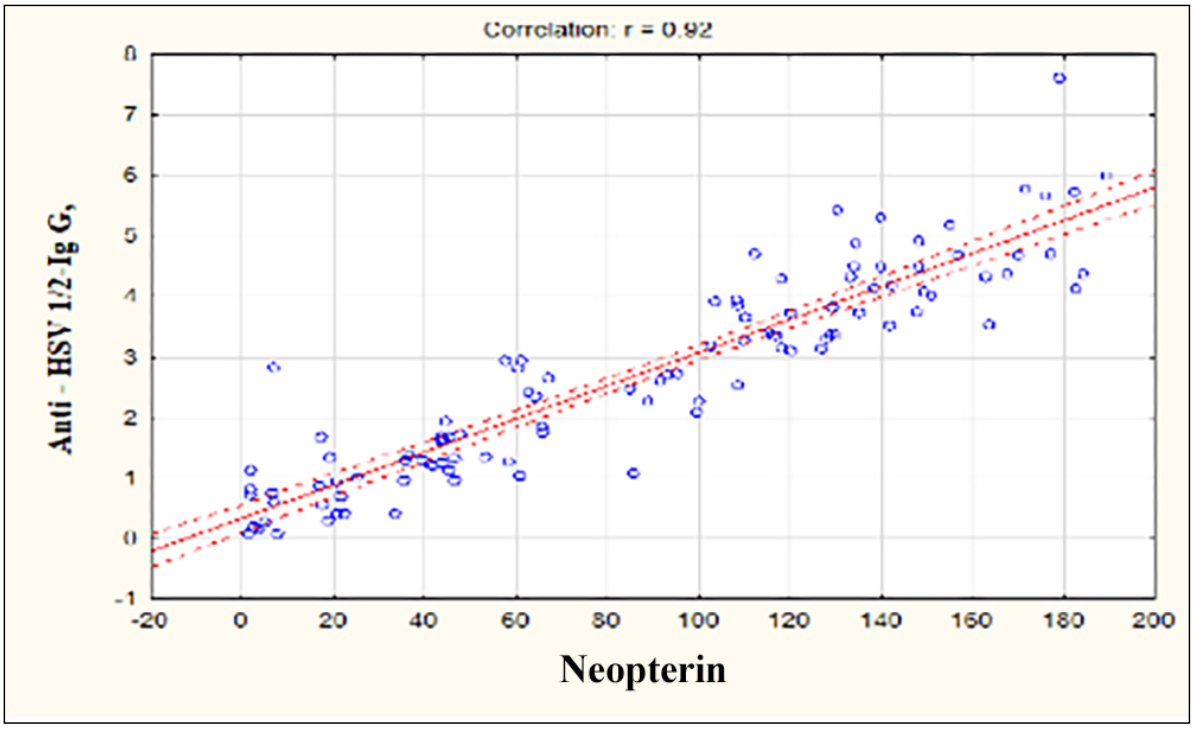

Fig. 4. Correlation between the level of Anti-HSV 1/2-IgG in the blood of mothers and the concentration of neopterin in the blood of newborns.

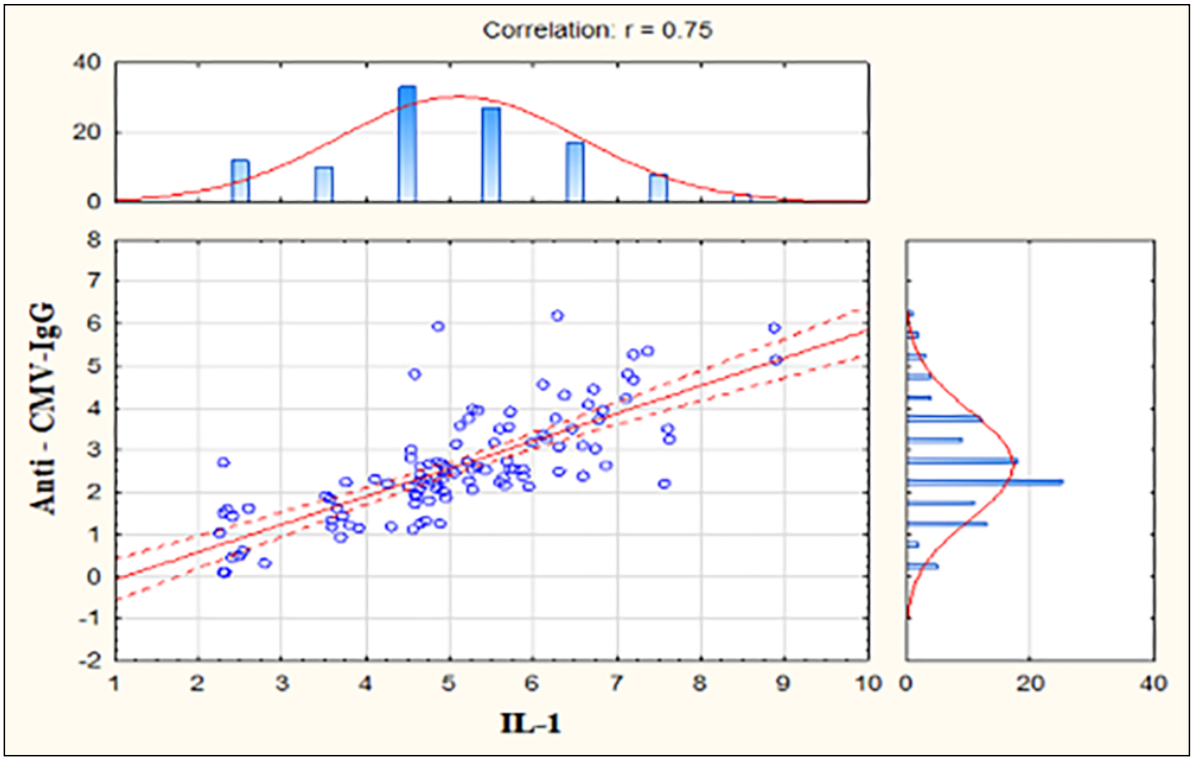

Fig. 5. Correlation between the level of Anti-CMV-IgG in the blood of mothers and the concentration of IL-1 in the blood of newborns.

studies, leads to diagnostic errors in 90-95% of cases [9, 10]. The identification of the causative agent itself is not enough to diagnose active IUI. Determination of cellular or humoral immunity does not provide an opportunity to adequately predict the risk of IUI at all stages of gestation. After the release of cytokines, the inflammatory reaction is realized in typical pathological processes, which mainly depend not so much on the type of the pathogen as on the gestation period, when the infection was realized. The study of cytokine

Table 5. Parameters of IgG levels to TORCH-infections in pregnant mothers

Parameters (n=109)	M±m	Min	Max
Anti-Toxopatoplasma-IgG, IUO/ml (>8,0)	100,67±	1,36	423,00
Anti-CMV-IgG, IU/ml (>0,9)	2,62±1,27	0,11	6,18
Anti-HSV ½-IgG, IU/ml (>0,9)	2,73±1,66	0,08	7,63

Table 6. Correlations between levels of Anti-Toxoplasma-IgG, Anti-CMV-IgG, Anti-HSV 1/2-IgG in mothers and laboratory parameters in infants

Parameters	Anti-Toxoplasma-IgG	Anti-HSV 1/2-IgG			Anti-CMV-IgG
IL-10	R= -0,27; p=0,004	Neopterin	r=0,92; p<0,001	IL-1	r=0,75; p<0,001
		TNF-α	r=-0,24; p=0,001	IL-10	r=-0,29; p=0,002

and interferon (IFN) status makes it possible to predict the implementation of infection in the early stages of pregnancy [11].

Cesarean section is the most common surgical procedure which performed in women of worldwide. The frequency of cesarean section should range from 10 to 15%? according to the recommendations of the World Health Organization (WHO) [12]. However, more and more often, women choose to give birth by cesarean section [13,14]. Perinatal mortality is up to 19 children per 1000, according to the world scientific literature [15]. In developed countries, is considered that this surgical intervention can prevent severe perinatal complications.

Respiratory and neurological disorders are more often observed in children borned by Caesarean section: autism spectrum disorders [16], schizophrenia [17]) and immune-dependent diseases [18,19], atopic dermatitis [20] and other childhood pathology [21]. The most common complications after cesarean section include the following: respiratory disorders, transient tachypnea, postpartum hypoglycemia [22,23]. Hansen et al. [24] announced data that the percentage of complications depends on the Caesarean section procedure and the length of pregnancy.

CONCLUSIONS

1. During a detailed analysis of the somatic and gynecological status of mothers high level of extragenital pathology in women in childbirth was observed due to diseases of the urinary system (21(19,2±2,4%) and diseases of the digestive system (18 (16,5±2,9%), thus indicating negative effects of TORCH infection on mothers and, potentially, on newborns. Reproductive dysfunction was detected in 51 (46,9%) mothers of children from the first and 10 mothers (32,3%) from the control group, significant differences were observed as for the number of miscarriages (26 (23,9±2,1%) vs. 3(9,7±2,2%), (p<0,001), confirming fetopathies, caused by TORCH infections in most cases.
2. Anti-Toxoplasma-IgG level (100,67 ± 94,67 IU/ml), which exceeded the upper limit of reference values by more than 12 times, Anti-HSV 1/2-IgG and Anti-CMV-IgG levels also exceeded physiological ranges up to 8 times.
3. Suppression of IL-10 level, as an anti-inflammatory factor in infants, is observed at high levels of Anti-Toxoplasma-IgG, as evidenced by the negative correlation between them (r=-0,27, p=0,004). The effect of Anti-HSV 1/2-IgG on the level of TNF-α has similar negative effects (r=-0,24, p=0,01). However, Anti-HSV 1/2-IgG does not have a negative effect on the level of neopterin in infants, on the contrary, it has a positive correlation (r=0,92, p<0,001), which indicates the absence of an effect on the inhibition of neopterin synthesis. The relationship between Anti-CMV-IgG and IL-1 (r=0,75, p<0,001) indicates the stimulation of the inflammatory process in premature infants and inhibition of IL-10 synthesis (r=-0,29, p=0,002).

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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