Agzamova Shoira Abdusalamovna,
MD, Department of Ambulatory Medicine
Tashkent Pediatric Medical Institut
E-mail: mbshakur@mail.ru

Factor analysis of cause-effect relationship of fetal infections of children by the agents of TORCH — complex

Abstract: A factor analysis of cause-effect relationships of fetal infection of babies by the agents of TORCH — complex (CMV, SHV 1, 2 types, Ch. trachomatis) was performed according to the results of clinical-laboratory, functional, immunologic, molecular-biologic and statistic research methods for new-born babies (216) in catamnesis up to 4 years old (116) and children from 20 days of life to 4 years old (202), born from mothers with chronic latent persistent TORCH infections and complicated by obstetric-gynecologic anamnesis.

Keywords: children of young age, fetal infection, TORCH — infections, cytomegalovirus, simple Herpes virus 1, 2 types, Ch. trachomatis, factor analysis.

The closest and remote complications of fetal TORCH infections and their latent-persistent progress often become the reason of deviations in young children's health and invalidization in elder age groups [1; 2; 3; 4; 5; 6].

TORCH- infections are one of the reasons of congenital defects of development, children's mortality and invalidity in childhood. According to official data in 2000 the infant lethality rate in Uzbekistan was 52 per 1000 alive born children, in 2002–62. Among them 8.9% were congenital abnormalities, 7% — fetal infections [1; 3; 7; 8].

The problems of TORCH infections impact on the health status and formation of a chronic pathology of various systems and organs in children, and immunological aspects of fetal infection realization are at the stage of study.

The aim of the study: is to perform factor analysis of cause-reaction links of fetal infection of children by the agents of TORCH — complex.

Materials and methods of the research. We performed a clinical monitoring of new-born babies (216 — main group) in catamnesis up to 4 years old (116) and children from 20 days to 4 years old (202 — comparison group), born by mothers with chronic latent-persistent TORCH infections and complicated obstetric gynecologic anamnesis for 2006–2010 period.. Etiologic diagnostics (by means of PCR, PCR-rt methods in real time, IEA) was done for 216 new-born babies and their mothers (130). 98 children who were infected intra uterine by cytomegalovirus (CMV), Simple Herpes virus 1 and 2 types (HSV) and Ch.trachomatis (Ch.t), we studied cell-mediated and humoral immunity with cytokine profile (IL-1β, IL-2 IL-8, IL-10, IFN-α).

419 children had cardiac rhythm graphic analysis with the study of spectral parameters of cardiac rhythm variability (CRV). Division of the children of the main group was done taking into account the agents of fetal TORCH infection:

I group — intra uterine infected by cytomegalovirus (CMV) (n=35).

II group — intra uterine infected by simple herpes virus 1 and 2 types (HSV 1 and 2 types) (n=27).

III group — infected intra uterine by Ch.trachomatis (n=10). The control group involved non-infected children (n=25).

In all these children (main group — 216 and comparison group — 202 children aged from 20–28 days to 4 years old with suspicion to FI, selected by means of randomization) we studied the risk factors of fetal infection and the results of complex clinical and para-clinical checking. For the construction of the model and the performance of the factor analysis the method of the main components was used. An optimal number of the isolated factors was defined taking into account Kaiser's criterion, «Scree-test» and factorization complicity degree, while all insignificant and non-identifiable factors of the model were united in so-called "zero" factor (F-0) [9; 10].

The results of the research and discussion. The factor analysis of CMV fetal infection impact provided the definition of five common factors to 73.5% of factorization complicity and "zero" factor to 26.5%.

The structure of the general factor impact on the realization of fetal CMV infection of children was presented (25.7%) by the action of the first (F-1: Factor of viral load) the most significant factor. The second factor according to its significance (F-2: CMV DNA factor in blood) defined about 14.9% of the impact on the outcome of infection. The influence of the rest 3 significant factors (F-3: LF Factor (power of low frequency part of the spectrum — slow waves 1st line or vasomotor waves, which characterizes the status of sympathetic part of VNS, and particularly the vascular tension regulation system); F-4: Speech development retardation Factor (SRF); F-5: Fetal development retardation factor (FRF), in the general structure of that factor model was conditioned by the parts from 12.4% to 9.8%.

In the analysis of the first factor impact (F-1, 25.7%) it was found out that the most significant factor load was supplied by high cytomegalovirus load in the blood samples of mothers of children infected intra uterine by CMV (–0.912). At the same time significant factor loads were noted for the value of positive PCR marker of CMV in blood and urine samples

among the mothers (–0.901), absence of pregravid preparation to pregnancy (–0.716), frequency of fetal-placental failure manifestations (negative Doppler metric symptoms), and that conditioned cause-reaction link of fetal CMV infection of children. Astenoneurotic — ANS (–0.802) and convulsive (–0.729) syndromes, functional disorders in intestine (–0.507) gain a specific actuality in the prognosis of fetal CMV infection outcomes, in the realization of which HF-1 (high frequency fluctuations, linked with respiratory waves and activity of parasympathetic nerve system) parameters convey high factor load (0.773), immune regulatory index — IRI (–0.765), IL-1β (–0.760), CD16+ (–0.590) IL-10 (–0.491).

The second factor defined by us according to its significance with the greatest impact on fetal infection, presence of CMV DNA in blood samples of the mothers (–0.889). Medical abortions (–0.686) and chronic colitis (–0.415) in mothers' anamnesis have the lower degree of factor load. Perinatal damages of CNS (–0.870), head and thoracic cage circumference ratio less than 1.0 (ГС<1.0 –0.564), later conditioning cognitive and verbal development of a baby, more often can become an outcome of fetal CMV infection.

Persistent character of the infection is determined by secretion of IL-8 (–0.746), big values of HF-1–1 (0.735), HF-1–5 (0.604), CD25+ (–0.708), IgM (–0.589), low values of CD4+ (-0.570). Secretion of F-3 factor (12.4%), interrelated with the value of LF (0.779), negative symptoms on neurosonography (–0.640), low rates on Apgar scale 6/7 points (–0.622), retardation of cognitive and motor development (–0.606), cerebral development defect (–0.586), myopia (–0.528), testify a possible interrelation of the main manifestation of fetal infection and CMV persisting.

Regular manifestation of F-4 impact (10.7%) determined the outcome severity for fetal CMV infection of children: verbal development retardation (0.773), angiopathy of retina (0.688), affect-respiratory paroxysms (–0.671), dysmetabolic nephropathy (0.551), low Ponderal index (0.489), chronic enterocolitis (0.453), conditioning high values in HF-2–3 sub-range (–0.618).

The threat of abortion (–0.560) in anamnesis and iron deficiency anemia in the mothers (–0.555) became the risk factors of fetal CMV infection of children. The action of the fifth factor F-5 (9.8%) united such manifestations of fetal infection as fetal development retardation (–0.695), defects of kidney development (0.631), in post-natal period infections of urinary ducts (–0.622), growth retardation in the age category "from birth to 6 months" (0.563). Cause-effect relationship of these states on mother side was exacerbation of pyelonephritis (0.577), chronic colpitis (–0.558) during pregnancy, body weight deficiency (BWI <19) (–0.495), and on the baby side — great values of IgG (0.511), CIC 4% (small circulating immune complexes containing IgG) (0.486).

The factor model of fetal HSV 1 and 2 types infection with factorization complicity 70.2%, was also represented by 5 factors. Great viral load HSV 1, 2 types in mothers' blood samples was the basis of cause-effect relationship for fetal infection by simple Herpes virus, and that determined the working title of the first factor F-1 (25.4%).

The complication of fetal HSV 1,2 types infection was perinatal damage of CNS (-0.870), convulsive syndrome (–0.629), RFD (–0.607), great amount of IL-8 (–0.578), low values of IRI (–0.565), CD4+ (–0.491), VLF-4 («very» low frequency fluctuations (slow waves 2 line), reflecting cerebral ergotropic impact on the lower levels and providing the data for judgment about the functional status of brain) (–0.690) and high density of spectral sub-range HF-1–22 (0.573). the risk factors of fetal infection were the following factor relevant to mother such as positive HSV 1 and 2 types marker in blood and urine samples (–0.870), only in blood (–0.811), and absence of pregravid preparation (–0.716).

Factor F-2 («Factor LF-1» — 14.1%) was determined by the factor load in LF-1 sub-range (–0.889), it was reflected in the values VLF-5 (0.708), HF-2–14 (0.735), HF-2–19 (0.604), CD20+ (–0.570) and it was related with the manifestations of frequent bronchial obstructive syndrome (–0.626), allergic-dermatitis syndrome — ADS (–0.615), ANS (–0.686), angiopathy of retina (–0.589), deficiency of weight (–0.564), VDR (–0.509). The presence of HSV 1,2 type DNA in urine samples determined the high factor impact on the fetal infection (–0.801).

The impact of the third factor F-3 («Factor CD23+» — 12.8%) displayed in the value of factor loads CD23+ (0.879), cerebral development defects (–0.635), Apgar scale (–0.622), retardation of cognitive and motor development (–0.610), defects of kidney development (–0.580), retardation of physical development in the age category "from birth to 6 months" (–0.540). Consequently, the parameters of LF-8 (0.583), HF-1–29 (0.471), HF-2–11 (0.422), HF-3–6 (–0.511) were diagnostically significant for the risk stratification of fetal HSV 1,2 types infection of children.

The analysis of the factor impact of F-4 («Early toxicosis factor» – 9.3%) showed the interrelation of that factor with early toxicosis of pregnant women (–0.787), chronic salpingooophoritis (–0.567), cervical erosion (–0.560), conditioning the high risk of fetal infection. Prognostically significant outcomes of fetal HSV infection were negative symptoms on neurosonography — NSG (–0.677), Ponderal index <60.0 (–0.509), great values of INF-α (–0.618), LF-20 (0.590), IL-10 (0.561), CIC 4% (0.488) and low values of IgA (–0.653).

Factor F-5 («Factor of transitory symptoms in new-born period» — 8.6%) was determined by factor load of transient manifestations syndrome during new-born period (–0.690). The most significant impact on the fetal HSV 1 and 2 types infection was characteristic for iron deficiency anemia — IDA (–0.522), one-parent family (0.513), father's low social-economic profession (–0.511), mother's age above 30 (0.504), matrimonial problems (–0.490). That risk was interrelated with the birth of premature babies (–0.579), high frequency of urinary infections — UI (–0.526) in children and it was associated by IgG high values.

The model of factor impact of fetal Ch. trachomatis infection (78.9%) had an isolated character. High risk of fetal Ch. trachomatis infection was conditioned by factor F-1 («Factor of positive PCR marker of Ch. trachomatis» — 26.1%), manifested in the positive PCR result of Ch. trachomatis (–0.902), UI (–0.870), cervical erosion (–0.802), endocervitis (–0.629) of mother, FRF (–0.607). Appearance of kidney development defects (–0.578), neutrophilosis with the drift to the left in new-born babies during the first day of life (–0.565), development of ANS (–0.690), UI (0.573), ENT-organs pathology (–0.491) in post-natal period, low values of ULF-2 (area of ultra low frequency, characterizing energetic balance and cortical regulation mechanisms, coordinating functional activity of all systems of organism) (–0.798), VLF-3 (0.716), LF-3 (–0.811) were prognostic factors of fetal Ch. trachomatis infection outcomes.

The analysis of F-2 («Factor of pregravid preparation» — 15.8%) displayed united impact of the pregravid preparation absence (–0.889), IDA (–0.870), exacerbation of pyelonephritis (–0.686), high water level (–0.564), chronic salpingoopharitis (-0.415) on the realization of fetal Ch. Trachomatis infection. The manifestation of action of fetal infection was mostly on the value of factor loads of VLF-5 (0.708), LF-18 (0.604), LF-20 (0.574), HF-1–17 (0.601), IRI (0.735), dysadaptation syndromes frequency (–0.746), FDR (–0.589), psychomotor retardation — PMR (–0.570).

The impact of the third factor F-3 («Factor VLF» — 14.4%) was determined for the values of very low frequency spectrum VLF CRV (0.879), with the highest factor load for NSG symptoms (–0.540), frequency of myopia manifestations (0.589), bronchial obstructive syndrome — BOS (–0.528) in children infected intra uterine by Ch. trachomatis. It was noted, that target impact of that factor on the prognostic values of infection risk changed under the influence of low frequency LF-20 activity (0.712), high frequency HF-2–22 (–0.681), HF-3–6 (–0.634) sub-ranges of CRV spectrum, and less due to the body weight value in the age category "from 6 months to 2 years" (0.610), severity of asphyxia according to Apgar scale (–0.580), relative and absolute amount of CD4+ (–0.511), CD8+ (0.422) and secretion of IL-8 (–0.471) in these children. The risk of fetal infection by Ch. trachomatis was determined by the severity of early toxicosis manifestations (0.635) and low water level (0.622) in pregnant women with chronic persistent TORCH — infection.

The forth factor F-4 («Factor CD95+» — 11.9%) had its effect to the values of lymphocyte activation marker CD95+ (–0.709), amount of IL-10 (0.509) and CIC4% (0.453), phagocyte activity of neutrophils (–0.477), determining, in its turn, conditions for Ch. trachomatis persisting in baby's organism. Greater manifestations of fetal infection and persistence of Ch. trachomatis was noted at the level of prevalence of convulsive syndrome (0.526) and physical retardation in the age category "from 6 months to 2 years" (0.517).

The fifth factor F-5 («Factor of dysmetabolic nephropathy — DMN — 10.7) was linked with the severity and frequency of dysmetabolic nephropathy manifestations (0.645), transient symptoms of new-born period (0.513), verbal development retardation (0.504) in children infected intra uterine by Ch. trachomatis. The risk of fetal infection by Ch. trachomatis was directly conditioned by social-demographic status of the family: mother's age above 30 (0.479) and one-parent family (0.422).

Conclusion. The factor analysis provided the isolation of the most significant factors determining the risk of fetal infection by the aforesaid agents and the possibility to prognoze its outcomes. The complex analysis of cause effect determining the risk of infection and original state of the infected children in catamnesis, on the basis of a common model helped us to isolate five the most significant factors for each infection with summary impact value 73.5%, 70.2% and 78.9%, correspondingly for CMV, HSV 1 and 2 types and Ch. trachomatis.

The greatest risk of fetal infection by CMV and HSV 1 and 2 types composed the "Factor of high viral load" (25.7% and 25.4%, correspondingly), and for Ch. trachomatis "Factor of positive PCR marker of Ch. Trachomatis" (26.1%), which determined the impact of the rest isolated common factors, integrally characterizing neurologic and somatic status of the children infected intra uterine.

The designed model of the factor analysis of cause-effect interrelationships of fetal and new-born infection by CMV, HSV 1 and 2 types and Ch. trachomatis let us optimize the measures taken for prophylactics and diagnostics of fetus and new-born babies' infection.

References:

1. Alimov B. D. Conditions of prevalence and manifestation of infections transmitted by sexual way (Chlamydia, Mycoplasma) in children, its diagnostics and therapy. Doctoral diss. – Tashkent, 2007. – 232 p.
2. Askarova S. V. Genital herpes and pregnancy//Bull. of Uzbekistan doctors association. – T., 2007. – № 1. – P. 96–98.
3. Asrankulova D. B. Perinatal secure of fetus and new-born baby in pregnancy with acute cytomegaloviral infection: Abstract of Doctoral diss. – Tashkent: 1st Tash. State. Med. Inst., 2004. – 31 p.
4. World health organization//Health and development of teenagers. – Copenhagen, 2005. – P. 23.
5. Nisevich L. L., Adiyeva A. A., Talalayev A., Kask L. Specific weight of fetal viral infections.//8th Russian Forum "Mother and child", Moscow – 2005, P. 581–582.
6. Frize K., Kakhel V., Kakhel K. Infectious diseases of pregnant women and new-born babies. M., Medicine, 2003. – 424 p.
7. Rakhmanova J. A. Prevalence of TORCH infections in the high risk groups and organization of anti-epidemic measures: Abstract of Doctoral diss. – MHC RUz, SRI of epidemiology, microbiology and infectious diseases. – T. 2007. – 21 p.

8. Babadjanova G. S. Pathogenetic aspect of reproductive function disorders, its correction and prognosis of healthy children in women with some kinds of chronic TORCH infections.//Doctoral disser. T. 2002. 285 p.
9. Blaghush P. Factor analysis with summary. – M.: Finances and statistics, 1989. – 248 p.
10. Borovikov V. P., Borovikov I. P. Statistica: Statistic analysis and processing of the data in Windows. – M.: IID " «Филинъ», 1997. – 608 p.

Azizov Bakhadyr,
Tashkent State Institute of Dentistry
E-mail: Dr.azizov@rambler.ru

Characteristics of the cellular immunity in HIV-infected patients with pyoderma

Immune system, being one of the major homeostatic systems, occupies the central place in the development of adaptation response to effects of the factors of an environment, with which the human body meets in the various periods of ontogenesis.

Pyoderma is one of the most widespread nosologies, accounting for to 40% of all cases of skin diseases [1]. Despite of distinctions in etiology, clinical picture, morphological changes and outcome, all pustular diseases, nevertheless, are unified by one common pathogenic mechanism — deviations in the immune system that has been confirmed by the numerous evidences [4; 5]. It is real, as the skin is considered as to be a component of immune system. As an immune organ it is capable of isolation, pressing, antigen presentation, production of immunoregulatory cytokines and development both of the local immune response and of the common, systemic to the antigens penetrating to the human organism. [9]. The high migration ability of the immune competent cells provides persistent connection of the skin to the central organs of immunogenesis. Any disorder of the skin integument integrity results in activation of immunocompetent skin cells providing elimination of local aggression and formation of immune memory [6; 8].

The lesions of skin and mucous environments at a HIV-infection are considered as the constant manifestations of the clinical picture, they occur in 84% of the patients [7]. From twelve AIDS-indicator diseases five apply to the skin pathology. In dynamics of HIV-infection the lesions of skin and mucous membranes have recurring character, with the periods of aggravations and remissions, and gain heavy, not peculiar to their clinic variants in the advanced forms of disease [10; 11].

In the patients with pyoderma with HIV-infection there are revealed various variants of immune deviations — from immune deficit to activation of some parameters in T- or B-cellular populations, which are interpreted differently. Some researchers state the point of view, according to which immune disorders are found only in the patients with heavy clinical course of dermatosis. At staphyloderma some authors note inhibition of T-cellular immunity, others — its activation [2; 3]. The similar data are received during study of humoral immunity at the various forms of pyoderma [12; 14].

The purpose of research was to study parameters of cellular immunity in HIV-positive patients with primary and secondary pyoderma.

Materials and methods. Under supervision there were 71 HIV-infected patients at the age of from 18 till 35 years, median was 27,7±1,3 years. The first group included 34 patients with the primary deep pyoderma, group two was constituted by 37 patients with secondary pyoderma. Group of the control consisted of 21 healthy volunteers, comparable by age and sex. The immunological investigations were performed on 1–2 day of admission to the hospital.

The immunological investigations were performed in the laboratory of immune cytokines of the Institute of Immunology of the Academy of Sciences of the Republic of Uzbekistan according to the methodical recommendations developed in the Institute of Immunology of the Ministry of Health of the Russian Federation and in the Institute of Immunology of the AS RUz (1992, 2001). Phenotype of immunocompetent cells was determined with use of monoclonal antibodies of the Joint Venture Ltd. "Sorbent" of the Institute of Immunology MH RF with method of indirect rosette using stabilized erythrocytes.

Results and discussion.

During study of HIV-infected patients with primary and secondary pyoderma at admission to the hospital there was observed tendency to the reliable reduction of the cellular immunity in comparison with healthy participants ($P < 0,001$). The results of study were presented in Table 1. The reliable differences between patients from group 1 and 2 were not found ($P > 0,05$).

In both groups of the patients the contents of relative and absolute parameters of lymphocytes was registered, on the average, reliably lower the control values ($P < 0,001$). We did not reveal reliable differences in the contents of lymphocytes in pyoderma, divided into groups depending on the clinical form of disease ($P > 0,05$).

Evaluation of the parameters of T-cellular immunity in the patients with HIV-infection, associated with secondary pyoderma, allowed to establish the tendency to decrease ($P < 0,001$) of relative T-lymphocyte counts with phenotype CD3 + (47,6±1,12%) in comparison with control group (59,3±1,1%).