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The Pharma Innovation

ISSN: 2277- 7695
TPI 2015; 4(6): 28-30

www.thepharmajournal.com
Received: 26-06-2015
Accepted: 29-07-2015

Kusa OM
Department of Obstetrics and Gynecology Ivano-Frankivsk National Medical University, Post Diploma Faculty Ivano-Frankivsk, Ukraine

Makarchuk OM
Department of Obstetrics and Gynecology Ivano-Frankivsk National Medical University, Post Diploma Faculty Ivano-Frankivsk, Ukraine

Correspondence:
Kusa OM
Department of Obstetrics and Gynecology Ivano-Frankivsk National Medical University, Post Diploma Faculty Ivano-Frankivsk, Ukraine

Role of Parvoviruses in Patological Pregnancies

Kusa OM, Makarchuk OM

Abstract
A clinical and clinical-laboratory examination of 130 women with viral and viral-bacterial infection verified at the stage of pre-gravid preparation was carried out. The control group consisted of 20 practically healthy women. We performed gynecological examination, reproductive and somatic history taking, bacterioscopic and bacteriological examination of vaginal contents. Infectious screening was carried out by identifying TORCH-group infections by enzyme immunoassay and polymerase chain reaction. Evaluation of parvovirus infection B-19 V was performed by identifying specific antibodies IgG and IgM using ELISA method. As a result, the study proved that patients in the study group - 41 women (31.53%) had no parvoviral symptoms of infection, 73 patients (82.02%) had characteristic symptoms at the planning stage of pregnancy long before the gestation. During ultrasound signs of uterine infection or threat of miscarriage in the first trimester - the antibodies to PV-B-19 (Ig G) were revealed in 68.46% of patients, 31.53% were seronegative, so they formed a group of high risk.

Keywords: parvovirus B-19, perinatal loss, intrauterine fetal infection, non- immune hydrops fetalis.

1. Introduction
At present in Ukraine there is epidemiological situation and activation of the prevalence of sexually-transmissible infections, which adversely affects the incidence, reproductive health and the probable perinatal loss [1]. Today it is proved that parvoviral infection leads to pathological pregnancies, but its serious impact on the health of patients with impaired hematopoiesis, especially on the background of gestation process is not studied enough. Distribution of parvoviral infection in Ukraine is not updated, information on typical seasonal outbreaks of this infection in our country is absent; the diagnostics of parvoviral infection during examination of pregnant women is not carried out. Many cases of miscarriages, fetal death, anemia, chronic arthritis and feverish conditions remain without installed etiology [2]. We think it happens because patients have low availability to such analyses and the physicians have little knowledge concerning this problem. Thus, literary analysis demonstrates that the role of microorganisms, including viral infection in the regulation of metabolism of sex steroids, and the importance of microbial endocrinology require further research in order to correct adequately not only hormonal disorders of the female reproductive system with a risk of fetal infection, but also to prevent placental dysfunctions. The aim of the research was to evaluate the role of parvoviral infection in the genesis of gestational complications.

2. Materials and methods of investigation
According to the purpose and objectives of the study we examined 130 women with viral and viral-bacterial infection verified at the stage of pre-gravid preparation. The control group consisted of 20 healthy women. The program included anamnesis, gynecological examination, bacterioscopic and bacteriological examination of vaginal contents. Infectious screening was conducted by bacterioscopic and bacteriological research and identification of TORCH-group infections by enzyme immunoassay and polymerase chain reaction. We estimated the contamination by parvovirus B-19V by identifying specific antibodies IgG and IgM using ELISA method. Mathematical methods were performed using the computer "Pentium-IV".

3. Results of the research and discussion
Today the problem of spreading of new virus - parvovirus B-19 is caused mainly by its asymptomatic course, increasing distribution, the lack of proper diagnosis and negative perinatal outcomes, all these factors has led to loss of control over the epidemiological situation [3]. Therefore, in the course of our study we decided to pay more attention to the diagnosis of the disease and search criteria of parvoviral infection because it is not studied enough and, as literary studies and our observations demonstrate, the most common in all

Study groups [4]. The most common symptoms of parvoviral infection in the studied groups were arthralgia and arthritis often combined with symptoms of acute respiratory viral infections with fever, pain in the throat and myalgia. More than half of women of the first and the fourth group (60% and 64% respectively) had such symptoms. Every second patient noted manifestations of chronic anaemia and liver dysfunctions, while such symptoms as idiopathic myocarditis, transient skin rash or aplastic crises happened very rarely, or weren't mentioned at all. In 45-50% of women parvoviral infection was asymptomatic. Almost all patients in the control group were practically healthy, the symptoms were observed in rare cases. Implementation of design studies revealed that patients in the main study group - 41 women (31.53%) had no symptoms of parvoviral infection; 73 patients (82.02%) had characteristic symptoms at the planning stage of pregnancy or long before the gestation; 25 (19.23%) pregnant women had such symptoms in the first half of pregnancy; 11 (12.35%) patients had the symptoms before probable impregnation. Modern investigations indicate that the level of activity of parvoviral infection in mother depends on her state of immunity, and the severity of the fetus affecting depends on the onset of the disease during pregnancy. In our study, at the stage of screening (pregestation period and the first trimester), including the symptoms of uterine infection or threat of miscarriage revealed with the help of USI in 89 (68.46%) patients antibodies (Ig G) to parvoviral infection were revealed, 41 women (31.53%) were seronegative. This group was at high risk. It should be mentioned that the negative results of the IgM study do not except intrauterine infection of the fetus, so for these patients it is advisable to perform simultaneous identification of DNA pathogen by PCR. The examination of blood serum in newborns (whose mothers belong to the main group) showed the following data: the serum in cord blood of newborns from women belonging to the main group contained significantly higher level of IgG in comparison with their mothers, while IgM was noticed in isolated cases, mainly in the group of patients with non-immune fetal hydrops.

As the literature sources show, the course of parvoviral B-19 infection depends on gestational term mainly. Fetal death rate is about 15% if the woman was infected in the first trimester of her pregnancy, especially during the first 8 weeks when she does not even know about her pregnancy. However, in the 2-nd trimester a fetus is very vulnerable to the virus because of the rapid increase of erythrocytes, short period of their life that may lead to massive haemolysis of red blood cells turning into the development of hepatic hemochromatosis. After the 20th week of pregnancy, the frequency of reproductive losses is 2.3%. Typically, fetal death occurs 1-10 weeks after the onset of symptoms in pregnant woman [5]. In 70-80% of cases when mother's infection is serologically confirmed, fetus does not die, that can be explained by virus neutralization with the help of antibodies. Non-immune hydrops fetalis occurs with a frequency of 1:3,000 - 1:4,000 pregnancies. Parvoviral infection is one of the most common causes of its development (18-27%). However, it should be noted that the risk of fetal hydrops in case of acute B-19 virus infection during pregnancy is small - about 1% only. Contamination of a fetus occurs only in 1/4 cases when the mother is infected [6]. Peculiarities of serological results for the presence of immunoglobulin G and M at the stage of screening lead to the necessity of analysis of perinatal outcomes in women who have non- immune hydrops fetalis.

In women with the risk of parvoviral infection, early and late reproductive losses at the stage of screening 3.5 times more frequently observed; 4 times more often babies are born dead or have deficiency of body weight. Fetal distress during pregnancy and childbirth against the indicators in the group having immunity to parvoviral infection ($p < 0,05$) should be associated with more severe manifestations of placental dysfunction and associated conditions for running disadaptation processes of fetoplacental complex. Lack of immune protection to parvovirus B-19 led to the increasing risk of premature birth: 21 women ($51,22 \pm 5,91$)% from the group of pregnant women without immunity to PV B-19 against 15 patients ($16,85 \pm 7, 10$)% from the group with the presence of Ig G to RV B-19. The most common cause of operative delivery in the group of women with lack of immunity to parvoviral infection were factors associated with fetal suffering caused by adverse intrauterine conditions (Doppler critical indicators).

4. Conclusions

One of the most dangerous and least studied infections is parvoviral infection. According to studies, endemic parvoviral infection is met much more frequently than believed as antibodies against the causative agent can be detected in 50-70% of patients. PV B-19 is one of the infections that may adversely affect pregnancy, cause development of fetal pathology and increase the number of perinatal losses. In our study, we revealed antibodies (Ig G) to parvoviral infection in 68.46% of patients in the main groups, 31.53% of women were seronegative. This group was at a high risk, as in the case of infecting of seronegative women during pregnancy in 20-30% of cases there is a risk of termination and intrauterine fetal infection with the following negative consequences. Study of peculiarities of pregnancy in women with parvoviral infection who have the risk to be infected by parvovirus because of the lack of immunity showed that this category of patients has big chances of getting negative perinatal consequences, various congenital malformations in their children, low weight in newborns, fetal distress and stillbirth, and a significant percentage of premature births ($p < 0.05$). So, our studies indicate the need for classification of women with mixed infection and women who have the risk of parvovirus B-19 infecting at the stage gestation to the group of high risk for the implementation of reproductive function and development of perinatal losses.

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