Prevalence of Parvovirus B19 Specific Antibody in Pregnant Women with Spontaneous Abortion

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Abstract- Human parvovirus B19 is a very common viral infection especially in school-aged children. The infection during pregnancy can affect the fetus due to lack of mother's immunity. Although, there is still no evidence of fetal teratogenic effects with parvovirus B19, but non-immune fetal hydrops and abortion may be caused by vertical transmission of the virus during pregnancy. This study was aimed to assess the prevalence of parvovirus B19-specific antibody (IgM) in pregnant women who had a spontaneous abortion. This cross-sectional study was carried out in all pregnant women who referred due to a spontaneous abortion. All demographic information such as age, occupation, and gestational age, last history of abortion, gravity, and presence of children below the age of six was recorded and a blood sample was provided for all the women. Then, the blood samples were tested to assay parvovirus B19-specific antibody (IgM) by EuroImmune ELISA kit. Among 94 pregnant women with the mean age of 28.4 years who had a spontaneous abortion, parvovirus B19 specific antibody (IgM) was detected in 17 participants (18.1%). Meanwhile, 14 women (14.9%) were suspected for presence of the antibody in their blood sample. There was no significant difference between the presence of antibody and age of pregnant women, occupation, gestational age, number of previous abortion, presence of children below the age of six and number of pregnancy. These findings revealed that a high percentage of pregnant women are probably non-immune against parvovirus B19, and also there might be a number of spontaneous abortions in which parvovirus infection caused fetal death. However, more studies are needed to prove the absolute role of parvovirus B19 in these abortions.

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Introduction

Parvovirus B19 is an uncoated DNA virus (1). Infection with this virus is common, and it differs from mild erythema infectiosum in children and leads to aplastic crisis, chronic hemolytic anemia and fetal death in pregnant women (2).

Parvovirus B19 is transferred through respiratory secretions. It can be transmitted to the child from the mother through blood and infectious blood products (3). If the mother has B19-specific antibodies (IgG) against the virus, there will be no possibility of virus transition to the fetus (4).

When mother is infected with the virus, viremia, presence of the virus in the blood, reaches its maximum level within a week. In 50% of cases, 10 -14 days after the infection, symptoms like erythema infectiosum, mild fever, headache, and impatience may be seen. Transition of virus from the mother to the fetus is estimated about 25%. The maximum possibility of virus transition is a week after the infection, when there is the maximum concentration of virus in mother's blood, and then IgM antibody starts appearing in circulation (4,5).

By increasing gestational age, the incidence of infection and fetal death decreases (3,4).That is because of passive transmission of antibody to the fetus in week 25 of pregnancy and after that, and decrease in appearing of P-antigen or globaside in villous trophoblast layer with an increase in gestational age as well (6,7).

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Almost in one third maternal parvovirus infections, a vertical transmission to the fetus occurs. Fetal infection with parvovirus associates with abortion, non-immune fetal hydrops, stillbirth and cerebral infection (8).

Infection is more common in spring season and major epidemic breaks out every four years (9).

Recovery from infection occurs when IgM antibody is produced for 10-12 days after the infection. IgM antibody remains for 3-6 months. IgG antibody can be recognized few days after appearance of IgM that remains for a lifetime, and it will cause natural immunization (8).

There is neither any accepted vaccine for Human Parvovirus nor is there any evidence to show that antivirus treatment prevents maternal or fetal infection. Although different studies concerning parvovirus infection were conducted in Iran among different groups of pregnant women, infants, young married women and blood donors, no study is conducted to assess the incidence of infection with Parvovirus B19 in pregnant women who had abortion. Thus, because of significant importance of parvovirus infection during pregnancy, the present study was designed to determine infection status of Parvovirus B19 in pregnant women who had a spontaneous abortion.

Materials and Methods

In a cross-sectional study from September 2011 to August 2012, all hospitalized pregnant women with spontaneous abortion were enrolled in the study.

Venous blood samples were collected from all participants after the abortion and parvovirus IgM titer was measured by ELISA method. All demographic information including age, occupation, gestational age, previous history of abortion, number of pregnancy and children under six years old were recorded.

After the separation of serum from blood samples, it was kept in -20°C freezer and IgM antibody against Parvovirus B19 was measured by EuroImmune ELISA kit. This kit has 100% sensitivity and specificity of 97%. It has not any crossover reaction with specific antibody against other viruses including CMV, EBV, HSV, measles, mumps, rubella, and VZV.

This test is semi-quantitative. According to manufacturer instructions, all ratios less than 0.8 was considered negative and the ratio equal or more than 1.1 was considered positive. The samples with a ratio between 0.8 and 1.1 ($0.8 \leq \text{sample} \leq 1.1$) were considered as suspicious, and a retest was then performed. If the sample's ratio was between 0.8 and 1.1 again, that sample was also considered as suspicious. In these participants, another blood sample was collected from the patients one week after the first sampling and both samples were tested again. However, because there was no chance of re-sampling in this study, serum samples of all patients were tested simultaneously. As a result, those samples were considered as suspicious.

The data was analyzed by chi-square, fisher and logistic regression test (at significant level %5) by SPSS16 software.

Results

A total of 94 pregnant women with an abortion were evaluated for prevalence of parvovirus specific antibody and 63 (67%) women had negative result, 14 (14.9%) women were suspicious and 17 (18.1%) women positive.

Afterward the relation of parvovirus specific antibody with other variables such as age, occupation, and gestational age, gravity, previous history of abortion and presence of children under six years old was compared.

One patient (4%) under 25 years old, 8(25%) patients between 25-29 years, 3 (14.3%) patients in 30-34 years old group and 5 (31.3%) patients in 35 years and older group had positive result for Parvovirus specific antibody that difference was not significant (P=0.091).

The minimum and maximum ages of women in this study were 18 and 45 years, respectively. The mean age was 28.4 years.

Four (4.2%) participants were employed, and 90 were unemployed. The incidence of Parvovirus specific antibody in unemployed women was 16.7% (15 cases) and in other occupations was 50% (2 cases) (P=0.148). There was no significant difference between the women's occupation and the positive result for Parvovirus specific IgM antibody.

Five (25%) participants with a child under six years old, and 12 (16.2%) without a child younger than 6 years old had positive result for Parvovirus specific antibody that difference was not significant (P=0.365).

Four (19%) women with a history of abortion and 13 (17.8%) without any history of abortion had a positive result for Parvovirus specific antibody. The difference between abortion and the incidence of Parvovirus specific antibody was not significant (P=0.897).

Twelve (21.4%) of 56 participants with a gestational age below 12 weeks and five (13.2%) of 38 women with gestational age of 12 weeks or more had Parvovirus

specific antibody. The association between gestational age and the incidence of Parvovirus specific antibody was not significant (*P*=0.307).

Mean ± SD of gestational age of patients was 11.7 ± 4.2 weeks.

In this study, pregnant women were divided into three groups or more, according to gravidity. Although most of the positive antibodies were among those with more than three parities, the difference of these three groups was not significant.

The incidence of Parvovirus specific antibody was positive in 13.5% of participants with one pregnancy, 18.5% of women with two pregnancies, and 23.3% of women with three or more pregnancies (*P*=0.582) (Table 1).

To evaluate multiple variables regarding incidence of Parvovirus specific IgM antibody simultaneously, logistic regression was performed, and none of the variables had significant statistical difference.

Table 1. The incidence of Parvovirus specific IgM antibody in pregnant women who had an abortion, in terms of patients' information

Patient info.		Presence of Parvovirus specific IgM antibody			
		Negative	Suspicious	Positive	Total
Occupation	Unemployed	61 (67.8%)	14 (15.6%)	15 (16.7%)	90
	other	2 (50%)	0 (0%)	2 (50%)	4
Having a child under 6 years old	yes	14 (70%)	1 (5%)	5 (25%)	20
	no	49 (66.2%)	13 (17.6%)	12 (16.2%)	74
History of abortion	yes	13 (61.9%)	4 (19%)	4 (19%)	21
	no	50 (68.5%)	10 (13.7%)	13 (17.8%)	73
Gestation age (week)	<12	37 (66.1%)	7 (12.5%)	12 (21.4%)	56
	≥ 12	26 (68.4%)	7 (18.4%)	5 (13.2%)	38
Gravidity	one	26 (70.3%)	6 (16.2%)	5 (13.5%)	37
	two	18 (66.7%)	4 (14.8%)	5 (18.5%)	27
	≥ 3	19 (63.3%)	4 (13.3%)	7 (23.3%)	30
Total		63 (67%)	14 (14.9%)	17 (18.1%)	94

Discussion

Parvovirus B19 is one of the most common viral infections in school-aged children that cause fetal infection in non-immune pregnant women (10). Although teratogenic effects of this virus are not proved yet (11,12), fetal infections during pregnancy cause 5-10% abortion (13,14), and 8-10% non-immune hydrops (15-18). Acute infection of Parvovirus B19 in pregnancy was recorded 1-2% that increases to more than 10% during an epidemic outbreak of the virus that happens every 3-6 years (19).

The present study showed that 18.1% of participants had Parvovirus B19 IgM specific antibody at the time of abortion which shows primary acute infection during pregnancy. It should be considered that 14.9% of participants were suspicious of infection with Parvovirus B19 because of the impossibility of re-sampling to confirm a definite diagnosis. Considering that acute infection with B19, parvovirus was observed in 18.1% of pregnant women. It seems that many pregnant women are not immune to this virus during pregnancy.

Recent studies in Europe have shown that a wide range of women in reproductive age is sensitive to the infection with Parvovirus B19 (from 26% in Belgium to 44% in Finland) (20). In another study, the percentage of non-immune pregnant women to Parvovirus B19 was estimated about 30 to 50 (10). In some studies conducted in Iran, the prevalence of infection is estimated to be 45% and 60% of reproductive age and pregnant women, respectively (21-23).

Variability of prevalence of the virus in acute primary infection may be due to the sampling methods, diagnostic methods, sample size, studied population, demographic and geographical variations season and, *etc.*

B19 virus can reach the fetus through placenta and cause fetal infection in 30 percent of maternal infections 10).

To determine how many abortions are due to infection with B19 virus in this study, it was necessary to show the virus DNA in fetal tissues by PCR method which was not the aim of current study, however, present findings may be a background for future studies in this field. Also in a study performed by Mirzaei *et al*., to determine the prevalence of Parvovirus B19 in IUFD (intra uterine fetal death), virus DNA was observed in 10 percent of participants (24). Riipinen *et al*., revealed that DNA of B19 Parvovirus was shown in 0.8% of abortions (25) and a study by Nymon *et al*., revealed

that it was observed in 3% of abortions in the first trimester and 12% in second trimester in fetal tissues (26). The incidence of specific IgM antibody in pregnant women was recorded as 2-5% (27-29), and it was 10% in Placental samples (30).

In a study by Jensen *et al*., in Denmark, a strong statistical association was observed between the presence of B19 IgM antibody during pregnancy and spontaneous abortion. It was reported that the percentage of spontaneous abortion in pregnant women with positive IgM antibody is 12.9% (31), and Miller et al. also found this association (13).

In current study, there is no significant correlation between the acute Parvovirus B19 infection in aborted pregnant women with age, occupation, and gestational age, history of abortions, gravity and having children under six years old; so these cannot be considered as risk factors for infection.

Zaki *et al*., reported that the detection rate of B19 Parvovirus specific antibody (IgM) in spontaneous recurrent abortion was significantly more than normal pregnant women. However, their study revealed that Parvovirus B19 is accompanied by recurrent spontaneous abortion and that serologic detection of B19 IgM antibody can be considered as a reliable screening test for high-risk pregnancies (7). It should be mentioned that in Zaki's study, 84% of pregnant women with recurrent spontaneous abortions were positive for parvovirus specific antibody IgM.

Jensen *et al*., during an epidemic outbreak of Parvovirus B19 among 3596 pregnant women in Denmark, reported that there is a significant association between acute infection of Parvovirus B19 (diagnosed by the presence of IgM antibodies or an increasing of IgG antibody titer during pregnancy in non-immune women) and having a child under the age of three or a high-stressed occupation and a life threatening disease that may be related to an increase in probability of acute infection in pregnant women as a result of the above three mentioned factors (31).

It should also be considered that the nature of these two studies is different to the present study in some way.

In conclusion, the fact that 18.1 percent of studied participants had specific Parvovirus B19 IgM antibody revealed a high prevalence of primary acute Parvovirus infection. Considering the potential role of this virus in abortion and fetal death, it emphasizes the importance of Parvovirus infection in pregnant women. Since no vaccine exists against this virus, further study is required to answer this question: Is it necessary to check pregnant women's immunity against B19 virus?

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