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Original Article

Viral-Induced Inflammation Can Lead to Adverse Pregnancy Outcomes

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Abstract

Introduction: Parvoviruses are DNA viruses of small size. There have been a number of reports indicating the possible effects of B19 infections during pregnancy. These effects include spontaneous abortions, stillbirth, fetal damage, and quite often, fetal anemia with hydrops fetalis.

Aim: The aim of this study was the correlation of Epstein-Barr virus (EBV) and parvovirus-B19 infections with inflammation levels in placental tissue coming from spontaneous abortions and elective terminations cases. We also investigated whether viral presence could cause spontaneous abortions by associating the expression levels of inflammatory markers with adverse pregnancy outcomes.

Materials and methods: One hundred ninety-four placental samples were used, 152 included in the study group coming from spontaneous abortions while 42 controls were used from cases of elective terminations. Hematoxylin and eosin (H&E) staining was performed to investigate morphological changes in the tissues, and then indirect immunohistochemistry to evaluate the expression of TNF-α, IL-6, IL-1α, B19, and EBV. Statistical analysis was performed using SPSS v. 19.0 (IBM).

Results: Higher inflammation levels were observed with statistical significance in the spontaneous abortions group ($p<0.001$) and they were correlated with statistical significance with B19 or EBV presence ($p<0.001$). Viral presence was only found in the spontaneous abortions group. Both simple and multiple logistic regression confirmed that viral presence was an independent prognostic factor for high expression of all inflammatory biomarkers with statistical significance ($p<0.001$).

Conclusions: Our results clearly indicate a specific pattern. Viral presence can deregulate inflammatory processes in the maternal-fetal environment and thus work as a trigger for spontaneous abortions.

Keywords

B19, EBV, pregnancy, spontaneous abortion, virus

INTRODUCTION

Parvoviruses are DNA viruses of small size. There have been a number of reports indicating the possible effects of B19 infections during pregnancy. These effects include spontaneous abortions, stillbirth, fetal damage, and quite often, fetal anemia with hydrops fetalis.[1-5] Parvovirus B19 infects mostly erythroid progenitor and myocardial cells, as well as the placental trophoblast and the fetal liver.[6] Infection from parvovirus B19 is globally present, infections peak throughout the spring months, while epidemics of a larger scale tend to occur on a 4-year cycle.[7] As far as pregnant women are concerned, the rate of infection is relatively low and changes from place to place; however, during epidemics, the incidence can rise up to higher than 10%.[8,9] Considering the above-mentioned findings, we can conclude that 20-50% of women of childbearing age had no contact with the virus, thus do not possess IgG specific-antibodies against B19V.[10-12] In the case of maternal infection, there is a high probability of fetal transmission of the virus, which can in turn cause adverse pregnancy outcomes[13,14] such as hydrops fetalis (HF)[15,16]. The Epstein-Barr virus (EBV) belongs to the herpes family, which comprises 9 viruses in total. EBV is one of the most common viruses in humans. The virus has been linked to a variety of diseases with the most known being infectious mononucleosis.[17-19] Transmission of the virus usually occurs through saliva but can also be transmitted through genital fluids.[20] Concerning congenital EBV infection, both the reactivation[21] and primary infection with EBV have been shown to cause fetal and neonatal disease, as it has been proven that both viruses show tropism for placental trophoblasts. However, there is a shortage of information about how EBV affects pregnancy outcomes, and its correlation with spontaneous abortions.[22,23] Pregnancy was considered as an anti-inflammatory response through the years, but later studies have shown that it actually is a process with distinct immunological stages.[24-26] So, the early stages of pregnancy (implantation and placentation) through the first and the early second trimester are considered pro-inflammatory, while the rest of the pregnancy up until the delivery is characterized as an anti-inflammatory state. Lastly, labor onset is also a process mediated by another inflammatory reaction.[27-30]

AIM

Our aim was to correlate Epstein-Barr virus (EBV) and parvovirus-B19 infection with inflammation levels in placental samples coming from spontaneous abortions, indicating that the overexpression of inflammatory proteins triggered by the viral presence can lead to an adverse pregnancy outcome.

MATERIALS AND METHODS

Samples

We used 152 placental samples from spontaneous abortions and intrauterine deaths from all three trimesters as a study group and 42 samples coming from pregnancy terminations in first and second trimesters of seemingly healthy fetuses as a control group.

All histological samples came from the archive of the Laboratory of Histology and Embryology of Democritus University of Thrace.

Staining

According to the standard histological protocol, all samples were fixed in 10% buffered formalin and embedded in paraffin. 3-μm hematoxylin-eosin-stained sections were histopathologically examined. Serial sections from each case were deparaffinized, rehydrated, and treated with 0.3% H_2O_2. Immunohistochemical staining was performed using the following antibodies: anti-IL-1α (Santa Cruz, Texas, USA-Mouse Monoclonal, 1:200), anti-IL-6 (Santa Cruz, Texas, USA, Rabbit Polyclonal, dilution 1:500), anti-TNF-α (Acris, Herford, Germany, Rabbit Polyclonal, 1:200), anti-B19 (Dako, Glostrup, Denmark, Rabbit Polyclonal, 1:200 dilution, specific for the VP2 protein) and anti-EBV (Dako, Glostrup, Denmark, Rabbit Polyclonal, 1:150 dilution, specific for the LMP protein) and was visualized by the peroxidase method (Envision System, DAKO, Carpinteria, CA, USA) using EnVisionTM FLEX diaminobenzidine (DAB) chromogen.

Immunohistochemical evaluation

All samples were studied using a Nikon Eclipse 50i microscope with an integrated camera Nikon Digital Sight DS-L1 (Nikon Corporation, Tokyo, Japan). From each histological section, 5 high-power fields were randomly chosen. Evaluation of antibody expression was performed using a semi-quantitative system, where no expression was valued as 0 (<10% stained cells), low expression (10-30%) as 1 medium (30-70%) and high expression (>70%) as 2 and 3, respectively.

Statistical analysis

Statistical analysis of our data was performed using SPSS v. 19.0 (IBM). Qualitative characteristics of the patients were expressed as absolute and relative frequencies (%), while quantitative variables were expressed as median values ±1 standard deviation (SD). Investigation of the correlation between expressions of the tested markers with patient characteristics was performed using chi-square test. Evaluation of the possibility for positive expression of TNF-α, IL-1α, IL-6, B19, and EBV was done through calculation of Odds Ratio

(OR) and the corresponding 95% confidence intervals (CI) through simple logistic regression models. Investigation of independent prognostic factors for positive expression of the tested markers was performed using a multiple logistic regression test. All statistical tests were bilateral and the results were considered statistically significant for $p<0.05$.

RESULTS

Staining results are shown in **Fig. 1**.

The characteristics of the patient groups as well as expression levels of each inflammatory marker in the two groups are shown in **Table 1**.

IL-6 expression in the study group compared to patient characteristics

Correlation of IL-6 expression with clinical characteristics is shown in **Table 2**. Chi-square test showed that higher IL-6 expression correlated with statistical significance with higher maternal age ($p=0.001$), advanced stage of pregnancy ($p=0.003$), and with viral presence ($p=0.001$ for both viruses). High IL-6 expression (≥30%) in comparison with clinical characteristics is shown in **Table 2**. The chi-square test indicated that high expression of IL-6 was associated with higher age (>35 yrs of age) ($p=0.003$). We also proved that positivity for EBV or B19 greatly increased the possibility of high IL-6 expression, as we found 60% of B19 positive samples to have high IL-6 expression, while only 7.7% of the B19 negative samples showed high expression for the same marker ($p<0.001$). The results were similar for EBV presence, with 66.7% of positive samples also having high expression of IL-6 ($p<0.001$). Simple logistic regression

Table 1. Comparison of the demographic and clinical characteristics between the two sample groups

	Groups		*P* value
	Control	Study	
Age			0.908
<25	13 (31.0)	44 (28.9)	
26-34	18 (42.9)	63 (41.4)	
≥35	11 (26.2)	45 (29.6)	
Trimester			<0.001
1st	30 (71.4)	51 (33.6)	
2nd	12 (28.6)	58 (3 28.2)	
3rd	0 (0.0)	43 (28.3)	
Sex			0.203
Male	24 (57.1)	70 (46.1)	
Female	18 (42.9)	82 (53.9)	
B19			0.080
Negative	42 (100.0)	142 (93.4)	
Positive	0 (0.0)	10 (6.6)	
EBV			0.106
Negative	42 (100.0)	142 (93.4)	
Positive	0 (0.0)	9 (5.9)	
IL-6 expression			**<0.001**
Negative	27 (64.3)	7 (4.6)	
Low	14 (33.3)	53 (34.9)	
Medium	1 (2.4)	75 (49.3)	
High	0 (0.0)	17 (11.2)	
TNF-a expression			**<0.001**
Negative	30 (71.4)	6 (3.9)	
Low	11 (26.2)	59 (38.8)	
Medium	1 (2.4)	70 (46.1)	
High	0 (0.0)	17 (11.2)	
IL-1a expression			**<0.001**
Negative	33 (78.6)	2 (1.3)	
Low	8 (19.0)	66 (43.4)	
Medium	1 (2.4)	65 (42.8)	
High	0 (0.0)	19 (12.5)	

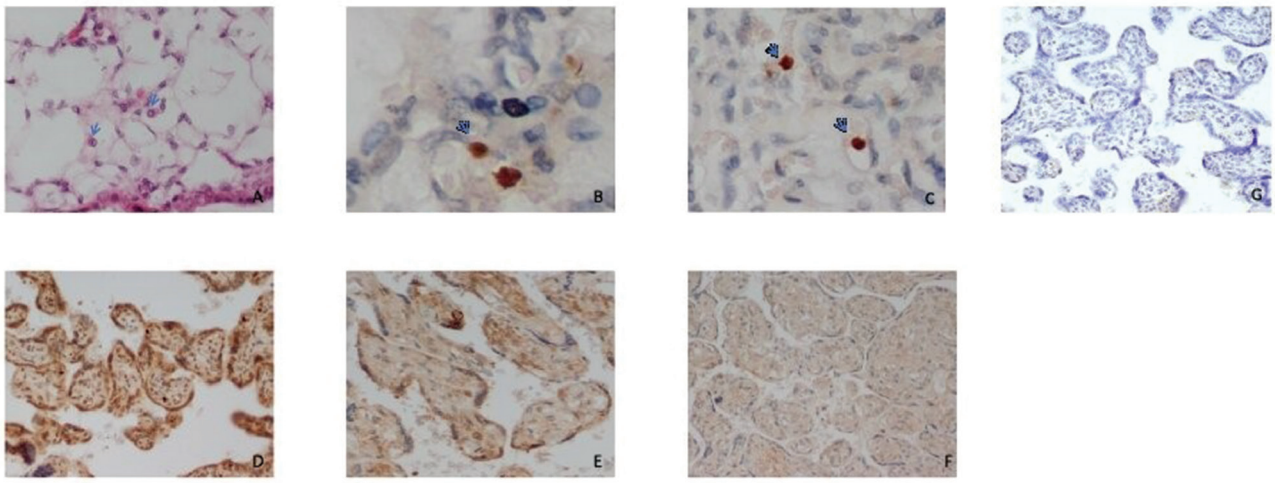

Figure 1. **A**. H&E staining in placental tissue coming from spontaneous abortions. Nuclear inclusion bodies indicated by arrows (×200); **B**. B19 positive IHC staining in placental tissue coming from spontaneous abortion indicated by arrow (×400); **C**. EBV positive IHC staining in placental tissue coming from spontaneous abortion indicated by arrows (×400); **D**. High expression of IL-6 IHC staining in placental tissue coming from spontaneous abortion (×200); **E**. High expression of IL-1α IHC staining in placental tissue coming from spontaneous abortion (×200); **F**. Moderate expression of TNF-α IHC staining in placental tissue coming from spontaneous abortion (×200); **G**. Negative marker in IHC staining (×200).

proved that positive IL-6 expression was 6.79 times more common in samples from patients who were over 35 years old (OR 6.79, 95% CI 1.41-32.76, p=0.017), 30.80 times more common in B19 positive samples (OR 30.80, 95% CI 6.89-137.69, p<0.001), and 24 times more common in EBV positive samples (OR 24.00, 95% CI 5.27-109.32, p<0.001). The multiple logistic regression test showed that the age of the mother (p=0.006), B19 (p<0.001), and EBV (p<0.001) presence remained independent prognostic factors for high IL-6 expression. Positive IL-6 expression was shown to be 5.88 times more common in higher ages (adjusted OR 5.88, 95% CI 1.68-20.66, p=0.006), 33.34 times more common in samples positive for B19 (adjusted OR 33.34, 95% CI 6.42-173.22, p<0.001), and 2.38 times more common in samples positive for EBV (adjusted OR 22.38, 95% CI 4.06-123.29, p<0.001) **(Table 2)**.

Table 2. Levels of IL-6 expression in the study group in comparison with clinical parameters. High IL-6 expression is associated with the demographic and clinical characteristics of the study group

	IL-6 expression				*p*-value
	Negative	**Low**	**Medium**	**High**	
Age					**0.001**
<25	4 (9.1)	23 (52.3)	15 (34.1)	2 (4.5)	
26-34	3 (4.8)	21 (33.3)	35 (55.6)	4 (6.3)	
≥35	0 (0.0)	9 (20.0)	25 (55.6)	11 (24.4)	
Trimester					**0.003**
1st	6 (11.8)	25 (49.0)	16 (31.4)	4 (7.8)	
2nd	1 (1.7)	15 (25.9)	36 (62.1)	6 (10.3)	
3rd	0 (0.0)	13 (30.2)	23 (53.5)	7 (16.3)	
Sex					**0.795**
Male	3 (4.3)	26 (37.1)	35 (50.0)	6 (8.6)	
Female	4 (4.9)	27 (32.9)	40 (48.8)	11 (13.4)	
B19					**<0.001**
Negative	7 (4.9)	53 (37.3)	72 (50.7)	10 (7.0)	
Positive	0 (0.0)	0 (0.0)	3 (30.0)	7 (70.0)	
EBV					**<0.001**
Negative	7 (4.9)	53 (37.3)	72 (50.7)	11 (7.7)	
Positive	0 (0.0)	0 (0.0)	3 (33.3)	6 (66.7)	

	Presence of high IL-6 expression					*p*-value
	No (%)	***p*-value**	**cOR (95% CI)**	***p*-value**	**aOR (95% CI)**	
Age		**0.003**				
<25	2 (4.5)		Ref.		Ref.	
26-34	4 (6.3)		1.42 (0.25-8.14)	0.691		
≥35	11 (24.4)		6.79 (1.41-32.76)	0.017	5.88 (1.68-20.66)	0.006
Trimester		0.419				
1st	4 (7.8)		Ref.		-	
2nd	6 (10.3)		1.36 (0.36-5.10)	0.653	-	
3rd	7 (16.3)		2.29 (0.62-8.41)	0.214	-	
Sex		0.345				
Male	8 (8.6)		Ref.		-	
Female	11 (13.4)		1.65 (0.58-4.73)	0.349	-	
B19		**<0.001**				
Negative	11 (7.7)		Ref.		Ref.	
Positive	6 (60.0)		30.80 (6.89-137.69)	<0.001	33.34 (6.42-173.22)	<0.001
EBV		**<0.001**				
Negative	11 (7.7)		Ref.		Ref.	
Positive	6 (66.7)		24 (5.27-109.32)	<0.001	22.38 (4.06-23.29)	<0.001

cOR: crude odds ratio; aOR: adjusted odds ratio; CI: confidence interval

IL-1α expression in the study group compared to patient characteristics

Correlation of IL-1α expression and clinical characteristics is shown in **Table 3**. The chi-square test showed that higher IL-1α expression was statistically correlated with higher age of the mother (p=0.03) and viral presence (p<0.001 for both viruses). Moreover, high expression of IL-1α (≥30%) was correlated with clinical characteristics **(Table 3)**. Using chi-square test, we found that high IL-1α expression was found with statistical significance more frequently in EBV or B19 positive samples (70% of them had high IL-1α expression, p<0.001). Simple logistic regression showed that IL-1α high expression was 13.91 more common in women of higher age (OR 13.91, 95% CI 1.71-113.15, p=0.014), 47.64 times more common in samples positive for B19 (OR 47.64, 95% CI 8.99-252.34, p<0.001), and 38.21 times more common in samples positive for EBV (OR 38.21, 95% CI 7.12-204.80, p<0.001). Finally, multiple logistic regression indicated that higher age (p=0.019), B19, and EBV presence (p<0.001) remained independent prognostic factors for high IL-1α expression increasing the risk by 4.16 times (adjusted OR 3.34, 95% CI 1.27-13.68, p=0.019), 49.16 times (adjusted OR 49.16, 95% CI 8.52-283.75, p<0.001), and 44.25 times (adjusted OR 44.25, 95% CI 7.70-254.32, p<0.001), respectively **(Table 3)**.

Table 3. Levels of IL-1α expression in comparison with clinical parameters. High IL-1α expression is associated with the demographic and clinical characteristics of the patients in the study group

	IL-1α expression				*p*-value	
	Negative	**Low**	**Medium**	**High**		
Age					**0.030**	
<25	1 (2.3)	18 (40.9)	24 (54.5)	1 (2.3)		
26-34	1 (1.6)	32 (50.8)	23 (36.5)	7 (11.1)		
≥35	0 (0.0)	16 (35.6)	18 (40.0)	11 (24.4)		
Trimester					0.462	
1st	1 (2.0)	25 (49.0)	20 (39.2)	5 (9.8)		
2nd	1 (1.7)	27 (46.6)	21 (36.2)	9 (15.5)		
3rd	0 (0.0)	14 (32.6)	24 (55.8)	5 (11.6)		
Sex					0.301	
Male	0 (0.0)	35 (50.0)	27 (38.6)	8 (11.4)		
Female	2 (2.4)	31 (37.8)	38 (46.3)	11 (13.4)		
B19					**<0.001**	
Negative	2 (1.4)	65 (45.8)	64 (45.1)	11 (7.7)		
Positive	0 (0.0)	1 (10.0)	1 (10.0)	8 (80.0)		
EBV					**<0.001**	
Negative	2 (1.4)	66 (46.2)	64 (44.1)	12 (8.4)		
Positive	0 (0.0)	0 (0.0)	2 (22.2)	7 (77.8)		
	Presence of high IL-1a expression					
	No (%)	***p*-value**	**cOR (95% CI)**	***p*-value**	**aOR (95% CI)**	***p*-value**
Age		**0.006**				
<25	1 (2.3)		Ref.		Ref.	
26-34	7 (11.1)		5.38 (0.64-45.35)	0.122		
≥35	11 (24.4)		13.91 (1.71-113.15)	0.014	4.16 (1.27-13.68)	0.019
Trimester		0.419				
1st	4 (7.8)		Ref.		-	
2nd	6 (10.3)		1.69 (0.53-5.42)	0.377	-	
3rd	7 (16.3)		1.21 (0.33-4.50)	0.775	-	
Sex		0.712				
Male	8 (11.4)		Ref.		-	
Female	11 (13.4)		1.20 (0.45-3.18)	0.712	-	
B19		<0.001				
Negative	12 (8.5)		Ref.		Ref.	
Positive	7 (70.0)		47.64 (8.99-252.34)	<0.001	49.16 (8.52-283.75)	<0.001
EBV		**<0.001**				
Negative	12 (8.4)		Ref.		Ref.	
Positive	7 (77.8)		38.12 (7.11-204.80)	<0.001	44.25 (7.70-254.32)	<0.001

cOR: crude odds ratio; aOR: adjusted odds ratio; CI: confidence interval

TNF-*α* expression in the study group compared to patient characteristics

Correlation of TNF-α expression with clinical characteristics is shown in **Table 4**. The chi-square test revealed that higher TNF-α expression was linked with advanced stages of pregnancy (p=0.016) and viral presence (p=0.001 for both viruses) with statistical significance. High TNF-α (≥30%) expression was then correlated with patients' characteristics as shown in **Table 4**. The chi-square test showed that 80% of B19 positive samples showed high TNF-α expression, while the same happened only in 5.3% of B19 negative samples. This indicates that high TNF-α expression is more common in samples positive for B19 infection with statistical significance (p=0.005). Results were the same for EBV infection as well, with 77.8% of positive samples having high TNF-α expression (p<0.001). Simple logistic regression showed that positive TNF-α expression was 59.11 times more common in B19 positive samples (OR 59.11, 95% CI 10.90-320.40, p<0.001), and 46.55 times more common in EBV positive samples (OR 46.55, 95% CI 8.52-254.25, p<0.001). Multiple logistic regression proved

Table 4. Levels of TNF-expression in comparison with clinical parameters. High TNF-α expression is associated with the demographic and clinical characteristics of the patients in the study group

	TNF-α expression				***p*-value**
	Negative	**Low**	**Medium**	**High**	
Age					0.075
<25	4 (9.1)	16 (36.4)	21 (47.7)	3 (6.8)	
26-34	1 (1.6)	31 (49.2)	25 (39.7)	6 (9.5)	
≥35	1 (2.2)	12 (26.7)	24 (53.3)	8 (17.8)	
Trimester					**0.016**
1st	5 (9.8)	25 (49.0)	16 (31.4)	5 (9.8)	
2nd	1 (1.7)	16 (27.6)	32 (55.2)	9 (15.5)	
3rd	0 (0.0)	18 (41.9)	22 (51.2)	3 (7.0)	
Sex					0.721
Male	3 (4.3)	26 (37.1)	31 (44.3)	10 (14.3)	
Female	3 (3.7)	33 (40.2)	39 (47.6)	7 (8.5)	
B19					**<0.001**
Negative	6 (4.2)	59 (41.5)	68 (47.9)	9 (6.3)	
Positive	0 (0.0)	0 (0.0)	2 (20.0)	8 (80.0)	
EBV					**<0.001**
Negative	6 (4.2)	59 (41.3)	68 (47.6)	10 (7.0)	
Positive	0 (0.0)	0 (0.0)	2 (22.2)	7 (77.8)	

	Presence of high TNF-a expression					***p*-value**
	No (%)	***p*-value**	**cOR (95% CI)**	***p*-value**	**aOR (95% CI)**	
Age		0.224				
<25	3 (6.8)		Ref.		-	
26-34	6 (9.5)		1.44 (0.34-6.09)	0.621	-	
≥35	8 (17.8)		2.96 (0.73-11.98)	0.129	-	
Trimester		0.375				
1st	5 (9.8)		Ref.		-	
2nd	9 (15.5)		1.69 (0.53-5.42)	0.377	-	
3rd	3 (7.0)		0.69 (0.16-3.07)	0.626	-	
Sex		0.262				
Male	10 (14.3)		Ref.		-	
Female	7 (8.5)		0.56 (0.20-1.56)	0.267	-	
B19		**0.005**				
Negative	9 (6.3)		Ref.		Ref.	
Positive	8 (80.0)		59.11 (10.90-320.40)	<0.001	55.08 (10.04-302.25)	<0.001
EBV		**<0.001**				
Negative	10 (7.0)		Ref.		Ref.	
Positive	7 (77.8)		46.55 (8.52-254.25)	<0.001	42.38 (7.39-242.97)	<0.001

cOR: crude odds ratio; aOR: adjusted odds ratio; CI: confidence interval

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viral presence as an independent prognostic factor for high (≥30%) TNF-α expression (p<0.001 for both viruses). To be exact, B19 raised the probability for positive TNF-α expression by 55.08 times (adjusted OR 55.08, 95% CI 10.04-302.25, p<0.001), while EBV - by 42.38 times (OR 42.38, 95% CI 7.39-242.97, p<0.001) **(Table 4)**.

DISCUSSION

Spontaneous abortion is pregnancy loss before 20 weeks gestation.[31] The percentages of spontaneous abortions are considerably high, indicating a crucial need to better understand the underlying pathology. Until now, several pathologies including chromosomal or genetic abnormalities have been proven as causes of spontaneous abortions.[32] Spontaneous abortions have also been linked with a variety of bacterial infections.[33] In the present study, we aimed to correlate viral presence with higher levels of inflammation markers as well as with pregnancy outcome. At first, we investigated the inflammatory biomarkers expression in the two samples' groups. Then we tried to indicate a possible association between viral presence and inflammatory biomarkers levels of expression in the spontaneous abortions group, in order to clarify the possible viral impact in the placental environment.

Until now, many studies have investigated the expression of different inflammatory markers in the placenta and any possible linked adverse pregnancy outcome.[34,35] Here, for the first time, we study comparatively a triplet of inflammatory markers in placental samples coming from all three trimesters and we report a statistically significant correlation with viral presence. These results can safely establish a relationship between B19 and EBV presence and elevated levels of inflammatory activity in the placentas coming from spontaneous abortions or intrauterine deaths. Our results are in accordance with other published studies, which investigated various viruses like B19, CMV, and Coxsakie virus and their correlation with spontaneous abortions.[36-38] It is also well known that elevated inflammation activity has been linked to spontaneous abortions.[39-41] Elevated amniotic fluid levels of IL-6 and serum levels of IL-1α have been confirmed as a causal factor for various adverse pregnancy outcomes such as preterm birth and premature rapture of membranes.[42,43] Deregulation of TNF-α serum levels has been linked with recurring fetal loss, gestation diabetes, fetal growth restriction and more pregnancy complications. [44] In our study, we confirmed these results in placental samples as well, proving a deregulation of their molecular pathways in the fetal-maternal environment. When all this is considered, we can safely conclude that pregnancy is widely affected by inflammatory processes that subsequently are tightly modulated during that period. Our research showed that viral infections could cause a deregulation of inflammatory cytokine levels in the maternal-fetal environment, which in turn have been linked to numerous adverse pregnancy outcomes.

CONCLUSIONS

Viral infections during pregnancy can trigger inflammatory pathways leading to elevated pro-inflammatory cytokine levels. These cytokines have been linked to various pregnancy complications including spontaneous abortions. However, further research is needed in order to establish if viral infections affect other molecular pathways involved with adverse pregnancy outcomes.

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Competing interests

The authors have declared that no competing interests exist.

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Вирусное воспаление может привести к неблагоприятным исходам беременности

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Резюме

Введение: Парвовирусы представляют собой ДНК-вирусы небольшого размера. Был ряд сообщений, указывающих на возможные последствия инфекций парвовирусом B19 во время беременности. Эти последствия включают самопроизвольные аборты, мертворождение, повреждение плода и нередко анемию плода с водянкой плода.

Цель: Целью данного исследования была корреляция инфекций, вызванных вирусом Epstein-Barr (EBV) и парвовирусом B19, с уровнем воспаления в плацентарной ткани, возникающим в результате самопроизвольных абортов и случаев планового прерывания беременности. Мы также исследовали, может ли присутствие вируса вызывать самопроизвольные аборты, связывая уровни экспрессии маркеров воспаления с неблагоприятными исходами беременности.

Материалы и методы: Были использованы сто девяносто четыре образца плаценты, 152 из которых вошли в основную группу, полученные от самопроизвольных абортов, а 42 контрольных были взяты из случаев планового прерывания беременности. Окрашивание гематоксилином и эозином (H&E) проводили для исследования морфологических изменений в тканях, а затем проводили непрямую иммуногистохимию для оценки экспрессии TNF-α, IL-6, IL-1α, B19 и EBV. Статистический анализ проводился с использованием SPSS v. 19.0 (IBM).

Результаты: Более высокие уровни воспаления наблюдались со статистической значимостью в группе самопроизвольных абортов (p<0.001) и коррелировали со статистической значимостью с наличием B19 или EBV (p<0.001). Присутствие вируса было обнаружено только в группе самопроизвольных абортов. Как простая, так и множественная логистическая регрессия подтвердила, что наличие вируса является независимым прогностическим фактором высокой экспрессии всех воспалительных биомаркеров со статистической значимостью (p<0.001).

Заключение: Наши результаты ясно указывают на определённую закономерность. Присутствие вируса может дерегулировать воспалительные процессы в материнско-фетальной среде и, таким образом, служить пусковым механизмом для самопроизвольных абортов.

Ключевые слова

B19, EBV, беременность, самопроизвольный аборт, вирус