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Original Article

Frequency of Human Parvovirus B19 Infection in Pregnancy.

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ABSTRACT

Background: Patients with established primary parvovirus infection are at risk of adverse pregnancy outcomes. In addition to the normal checkup for fetal hydrops or intrauterine mortalities, investigation of parvovirus B19 infection was advised.

Aim and objectives: The aim of the study is to assess the frequency of parvovirus B19 infection in cases of unexplained intrauterine fetal death, non-immune hydrops, and abortion.

Subjects and methods: This study was a cross-sectional study that included 60 female patients who suffered from unexplained intra-uterine fetal death, abortion or, non-immune hydrops during six months. All patients fulfilling the inclusion criteria were recruited from Obstetrics and Gynecology Department of Zagazig University hospitals and Suez Health Insurance Hospital. All participants were subjected to complete history taking with special emphasis on obstetric and prenatal history.

Ultrasound examination is performed for all participants to confirm IUFD, abortion or hydrops and to exclude other fetal anomalies not included in our study. We did other investigations including routine laboratory investigations in addition venous blood sampling for detection of human parvovirus B19 antibody IgM and IgG in these samples

Results: The presence of seropositive parvovirus B19 IgG was 43.3% and the presence of `parvovirus B19 IgM was 5%. Regarding the seropositivity for parvovirus B19 in the studied cases, there was no statistically significant difference between negative and positive groups.

Conclusion: The study showed that 48.3% of the women with unexplained intrauterine fetal death, abortion, or non-immune hydrops were seropositive for HPV B19.

Keywords: HPV B19, Obstetric, Pregnancy, Hydrops

INTRODUCTION

HPV B19 is a small seasonal variation with a spring resurgence**[1]**

In pregnancy, the prevalence of acute human parvovirus B19 (HPV B19) infection is around 1-2 percent, which can reach 10 percent during epidemic times. All through pregnancy, infection with HPV B19 is often symptomless for mothers and does not affect the fetus. Even then, mortality and morbidity can happen in immunocompromised pregnant women who suffer from pre-existing hematological problems or infected babies in which there is severe tissue and red cell breakdown. **[2]**

The virus may cause severe acute anaemia in patients with chronic hemolytic anaemia resulting in transient aplastic crisis [3]

B19 should be included in differential diagnosis of encephalitic syndromes of unknown etiology in all age groups **[4]**

Patients with established primary parvovirus infection are at risk of adverse pregnancy outcomes. Infection with parvovirus is a possible cause of negative pregnancy outcomes involving fetal hydrops, increased incidence of mortality, spontaneous abortion. **[5]**

Among the signs of congenital parvovirus infection is the elevated nuchal translucency and / or the existence of fetal hydrops during ultrasound assessment at the first trimester. Disturbed fetal hemodynamics stemming from moderate cardiomegaly, gradual increase in peak systolic velocity with in middle cerebral artery, redirected stream in ductus venosus throughout atrial

contraction and occurrence of hydrops have been documented in parvovirus infection studies throughout gestation. **[2]**

Middle cerebral artery peak systolic velocity (MCA-PSV) is a high sensitive non-invasive means for determining the degree of fetal anemia [6]

The incidence of maternal parvoviral seroconversion ranges from 3 percent to 34 percent and the chance of vertical transmission is nearly 30 percent. In scenarios of 0-12.5 percent of affected babies with a peak gestation among 17 and 24 weeks, fetal hydrops occur, however fetal death is bound to happen at a rate of 5-10 percent, even without the presence of fetal hydrops in scenarios of uncertain pathogenesis. **[5]**

Besides the normal work-up for fetal hydrops or intrauterine mortalities, investigations into HPV B19 infection were advised. It is especially hard to decipher the findings of IgM research. A better diagnostic method seems to be polymerase chain reaction (PCR). **[5]**

HPV B19 can also be transmitted by organ transplant in patient with bone marrow, liver and renal transplants[10]

AIM AND OBJECTIVES

the aim of the study was to assess the frequency of parvovirus B19 infection in cases of unexplained intrauterine fetal death, non-immune hydrops, and abortion.

SUBJECTS AND METHODS

Technical design:Study design: The present study was a cross-sectional study that included 60 female patients who suffered from unexplained intra-uterine fetal death, abortion or, non-immune hydrops during six months. All patients fulfilling the inclusion criteria were recruited from Obstetrics and Gynaecology Department of Zagazig University hospitals and Suez Health Insurance Hospital. We included adult females aged more than18 years old and with unexplained intra-uterine fetal death, first and second trimester missed abortions, or non-immune hydrops. We excluded patients with medical disorders as hypertensive disorders with pregnancy or diabetes, with previous diagnosis of TORCH infection, lupus anti-coagulant or anti-cardiolipin antibodies or with diagnosis or history of chromosomal abnormalities or fetal anomalies (other than hydrops fetalis).

Methods: All the studied groups were subjected to complete history taking with special emphasis on obstetric and prenatal history. Thorough clinical, obstetric, and neurological examinations were done. Ultrasound examination was performed for all participants to confirm IUFD, abortion or hydrops and other findings as gestational age and to exclude other fetal anomalies not included in our study. We did other investigations including routine laboratory investigations as complete blood count, liver and kidney function tests, urine analysis and immunological tests (if suspected). Also, the investigations included venous blood sampling for detection of human parvovirus B19 antibody IgM and IgG in these samples by using a third generation qualitative capture enzyme immunoassay (Diasorin-Biotrin;catalog no. V619IM and V619IG) that detect IgM and IgG antibody against human parvovirus B19 structural proteins.

The kit contained 3 standard controls S1, S2 and S3 that were used in interpretation of the results as recommended by manufacturer briefly;

Administrative considerations: Written informed consent was obtained from all participants and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University (Institutional Research Board IRB). The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

STATISTICAL ANALYSIS

An Excel spreadsheet was established for the entry of data. We used validation checks on numerical variables and option-based data entry method for categorical variables to reduce potential errors. The analyses were carried with SPSS software (Statistical Package for the Social Sciences, version 24, SSPS Inc, Chicago, IL, USA).

Numerical data were described as mean ±SD if normally distributed; or median and interquartile range [IQR] if not normally distributed. Frequency tables with percentages were used for categorical variables. Independent Student t-test and paired t-test were used to compare parametric quantitative variables. Chi-square tests were used to analyze categorical variables. A p-value < 0.05 is considered statistically significant.

RESULTS

Table (1) shows the demographic characteristics of the studied patients. The age of the included patients have a range (18-35) years; while the majority of them were from rural areas (61.7%). In addition, 33.3% of patients were categorized as high social class and 66.6% were categorized as low.

Table (2) clears the obstetric history for the participants. In term of obstetric history, the majority of the women were in their second trimester during abortions or non-immune hydrops occurrence. Most of the cases had one parity.

Table (3) demonstrates the IgG and IgM seropositivity for parvovirus B19 in the studied cases. The presence of seropositive parvovirus B19 IgG was 43.3% and the presence of parvovirus B19 IgM was 5%.

Table (4) reveals the association between seropositivity for parvovirus B19 and demographic data in the studied cases. The obtained results showed that there was statistically significant association between patients' age and seropositivity for parvovirus B19 (p = 0.002); patients with seropositive results were older than patients with negative results. On the other hand, there were no statistically significant associations between seropositivity for parvovirus B19 and residency (p = 0.96) or education level (p = 0.94). The obtained results showed that there was statistically significant association between patients' BMI and seropositivity for parvovirus B19

Table (5) clears the association between seropositivity for parvovirus B19 and obstetric history. There were no statistically significant associations between seropositivity for parvovirus B19 and gestational age (p = 0.07) or parity (p = 0.61).

Table (6) shows the association between seropositivity for parvovirus B19 and CBC findings. The obtained results showed that there were no statistically significant associations between seropositivity for parvovirus B19 and hemoglobin levels (p = 0.38), WBCs (p = 0.33), or platelet count (p = 0.42).

Table (7) reveals the seropositivity for parvovirus B19 in the studied cases. There was no statistically significant difference between negative and positive groups (P = 0.61). Seropositivity for HPV B19 was 53.3% in IUFD cases, 42.3% in cases abortions and 50% in cases of non-immune hydrops. Seven cases had abortions in the first trimester and 4 cases in the second trimester. Three cases of abortions were IgM positive. The patients were diagnosed as missed abortion at 10, 12 and 15 weeks.

Table (1): The demographic characteristics of the studied patients.

Variables	Patients (N =60)
BMI in Kg/m^2	
Mean ± SD	26.9 ± 4
Range	21 - 32
Age in years	
Mean ± SD	27 ±3.92
Range	18 - 35
Residency, No. (%)	
Urban	23 (38.3%)
Rural	37 (61.7%)
Social class, No. (%)	
Low	30 (50%)
mid	20 (33.3%)
High	10 (16.7%)

* Data are presented as mean ± SD, median (Range), or number (%).

Table (2): Shows the obstetric history for the participants.

Variables	weeks	
Gestational Age in weeks at time of inclusion,		
(Mean ± SD):		
Unexplained abortion: First trimester (N=15)	9±1.1	
Second trimester (N=11)	20±2.05	
Unexplained hydrops	25±2.16	
Unexplained IUFD	30±2.4	
	Patients	(N =60)
Parity, No. (%)		
1	24	(40%)
2	20	(33.3%)
3	13	(21.7%)
4	3	(5%)
History of previous abortion, No. (%)		
Yes	9	(15%)
No	51	(85%)
History of previous nonimmune hydrops, No. (%)		
Yes	4	(6.7%)

Variables	weeks	
No	56	(93.3%)
History of previous IUFD, No. (%)		
Yes	17	(28.3%)
No	43	(71.7%)

* Data are presented as mean ± SD, median (Range), or number (%).

Table (3): IgG and IgM seropositivity for parvovirus B19 in the studied cases.

Variables	Patients (N =60) N. & %
Seropositivity for parvovirus B19	29 (48.3%)
IgG	26 (43.3%)
IgM	3 (5%)
Seronegative for parvovirus B19	31 (51.7%)

* Data are presented as number and percentage.

Table (4): Association between seropositivity for parvovirus B19 and demographic data in the studied cases.

Variables	Positive (N=9)	Negative (N=31)	P value
Age in years Mean ± SD Range	 27 ± 4.26 23 - 35	 22.98 ± 3.58 18 - 31	0.002
Residency, No. (%) Urban Rural	 11 (37.9%) 18 (62.1%)	 12 (38.7%) 19 (61.3%)	0.96
Social class, No. (%) Low mid High	 16 (55.2%) 9 (31%) 4 (13.8%)	 14 (45.2%) 11 (35.5%) 6 (19.4%)	0.94
BMI in Kg/m2 Mean ± SD Range	 29 ± 4.2 26 - 32	 25 ± 3.9 21 - 27	0.005

*Data are presented as mean ± SD, median (Range), or number (%).

Table (5): The association between seropositivity for parvovirus B19 and obstetric history.

Variables	Positive (N =29)	Negative (N =31)	P-value
Gestational Age in weeks at time of inclusion, (Mean ± SD): Unexplained abortion: First trimester Second trimester Unexplained hydrops Unexplained IUFD	 7 4 2 16	 8 7 2 14	0.07
Parity, No. (%) 1 2 3 4	 14 (48.3%) 9 (31%) 5 (17.2%) 1 (3.4%)	 10 (32.3%) 11 (35.5%) 8 (25.8%) 2 (6.4%)	0.61

*Data are presented as mean ± SD, median (Range), or number (%). A p-value < 0.05 is considered statistically significant.

Table (6): Association between seropositivity for parvovirus B19 and CBC findings.

Variables	Negative (N =31)	Positive (N =29)	P-value
Hemoglobin (g/dL)			

Mean ± SD Range	11.2 ±2.2 8 - 14	11.7 ± 2.2 8 - 14	0.38
WBCs x103 (cell/mm3) Mean ± SD Range	 6.9 ±1.2 4 - 9.5	 7.2 ± 1.2 4 - 9.5	 0.33
Platelet (cell/mm3) Mean ± SD Range	 139214.2 ± 4138.8 100000 - 190000	 119214.2 ± 4138.8 100000 - 190000	 0.42

*Data are presented as mean ± SD, median (Range). A p-value < 0.05 is considered statistically significant.

Table (7): Seropositivity for parvovirus B19 in the studied cases.

Variables	Positive (N =29)	Negative (N=31)	P-value
Diagnosis, No. (%) Unexplained: IUFD (N=30) Abortion (N=26) First trimester Second trimester Non-immune hydrops (N=4)	 16/30 (53.3%) 11/26 (42.3%) 7 4 2/4 (50%)	 14 (45.2%) 15 (48.8%) 8 7 2/4 (50%)	 0.61

*Data are presented as mean ± SD, median (Range). A p-value < 0.05 is considered statistically significant.

DISCUSSION

There was a limitation in the study as it included only 60 female patients and we didn't follow cases of recent infection (positive IgM) for development of IgG antibodies. Cases of positiveHPV B19 IgM which developed non immune hydrops after 2-6 weeks, positive IgG would be detected in their serum by that time .

The most frequent natural fluctuations of HPV B19 is during winter, spring, and initial period of summer. A lytic infection of erythroid progenitor cells triggered by the virus contributes to the inhibition of hematopoiesis. **[7]**

Additionally, the incidence of HPV B19 in pregnant women is rare in the existing studies. Therefore, we conducted the present cross-sectional study in order to assess the frequency of parvovirus B19 infection in cases of intra-uterine fetal death, non-immune hydrops, and abortion.

The present study included 60 female patients who suffered unexplained intrauterine fetal death, abortion, or non-immune hydrops. Thirty (50%) cases had intrauterine fetal death, 26 (43.3%) cases had abortion, and 4 (6.6%) cases had non-immune hydrops. Regarding the primary outcomes of the present study, we found that the seropositivity for parvovirus B19 IgG was 43.3% and for parvovirus B19 IgM was 5%.

The mean age of the included patients was 27 ±3.92 years and the majority of the women were in their third trimester during fetal death. Most of the residency of the included patients was rural and most of them (66.6%) were categorized as low social class. Forty percent of the women had had one previous pregnancy, while only 5% had previous 4 pregnancies. The mean hemoglobin of the included patients was 11.7 ± 2.2 g/dL, and the average WBCs was 7.2 ± 1.2 x 1000 cell/mm2.

In this study, we found 16 cases (53.3%) positive for HPV B19 IgG which had IUFD in the third trimester with ages ranging between 23 and 35 years. In randomly selected cases of intrauterine mortalities, Tolfvenstam and colleagues evaluated the incidence of infection with HPV B19. The incidence of infection with HPV B19 throughout pregnancy was 15 percent. **[7]**

In our studied cases (N=60), there were 26 cases of abortion, 11 cases were positive for HPV B19, 7 of them were in the first trimester and 4 cases were in the second trimester. Eight cases (30.7%) were positive HPV B19 IgG, and 3 cases were IgM positive (11.5%). The cases with positive HPV B19 IgM had missed abortions at the 10, 12 and 15 weeks of gestation, so acute infection is high risky to the fetus. The rest of the cases were HPV B19 IgG positive which indicated infection more than 3 months when pathological process starts ending in abortion, IUFD or non-immune hydrops.

In the same line, Sorour and colleagues was aiming to evaluate the relationship between infection with HPV B19 and repeated spontaneous abortion, and to compare the serological diagnostic methods and PCR for the diagnosis of HPV B19 infection in patients of this type. In six percent of cases, HPV B19 IgM appeared to be positive, and in 62 percent of cases, HPV B19 IgG was reported to be positive. **[8]**

In this study, 4 cases had non-immune hydrops were included. We found 2 of them (50%) positive for HPV B19 IgG. A retrospective analysis of gathered clinical and laboratory findings from hydropic and anemic embryos, with a documented

HPV B19 infection during pregnancy, was conducted by Dehaan and colleagues. For quantitative HPV B19 viral load, fetal blood samples were examined. Positive fetal blood samples for HPV B19 antibodies with 100 percent congenital HPV B19 infection were found in all cases. **[9]**

CONCLUSION

The study showed that 48.3% of the women with unexplained intrauterine fetal death, abortion, or non-immune hydrops were seropositive for HPV B19,

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