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Pattern of Parvovirus B19 Infection During Different Trimesters of Pregnancy in Kuwait

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ABSTRACT

Objective: Aims of this study were to determine the IgG and IgM seropositivity to parvovirus B19 during the three trimesters of pregnancy.

Methods: Initially, a total of 1,047 pregnant women were included in a prospective study. Blood samples were obtained from 343, 406 and 298 cases in the first, second and third trimesters, respectively. To study the incidence of seroconversion, a second sample of blood was obtained 2–4 weeks later from the first 100 cases, who were IgG and IgM negative in the first trimester.

Results: The seroprevalence of parvovirus B19 IgG and IgM was 53.3% and 2.2%, respectively. The incidence of seroconversion was 16.5%. The rate of fetal loss was 15.4% in patients with acute infection, all of which occurred in the first two trimesters.

Conclusions: The percentage of IgG positive cases is significantly higher in first and second trimesters compared to the third trimester. The seroconversion rate was 16.5%. Infect. Dis. Obstet. Gynecol. 7:287–292, 1999. © 1999 Wiley-Liss, Inc.

KEY WORDS
parvovirus; seroprevalence; trimesters; pregnancy; Kuwait

Cossart et al. discovered the parvovirus B19 accidentally in 1975 while they were evaluating screening tests for the hepatitis B virus.[1] Parvoviruses are small, round viruses with a single-stranded DNA genome that lacks a lipid envelope. Infection with parvovirus B19 is usually spread by the respiratory route, but may be transmitted by blood components or blood products.[2] Parvovirus B19 has been implicated as a primary etiologic agent of erythema infectiosum (fifth disease) and aplastic crisis in patients with chronic hemolytic anemias.[3,4,5] It has also been associated with arthritis.[6,7]

Human parvovirus B19 is now a recognized cause of non-immune hydrops fetalis and intrauterine fetal death.[8,9,10,11] However, maternal parvovirus B19 infection is usually followed by a successful outcome with delivery of a normal infant. Since parvovirus B19 has a propensity for infecting rapidly dividing cells, particularly erythroblasts, the greatest risk to the fetus occurs during the first 20 weeks of pregnancy, and especially between weeks 10 and 20 which coincides with the major development of erythroid precursors.[12,13]

This study is aimed at studying the pattern of parvovirus B19 infection during different trimesters of pregnancy and the incidence of seroconversion in the obstetric population of Kuwait.

SUBJECTS AND METHODS

Initially, a total of 1,047 pregnant women were included in a prospective study which was conducted

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Clinical Study

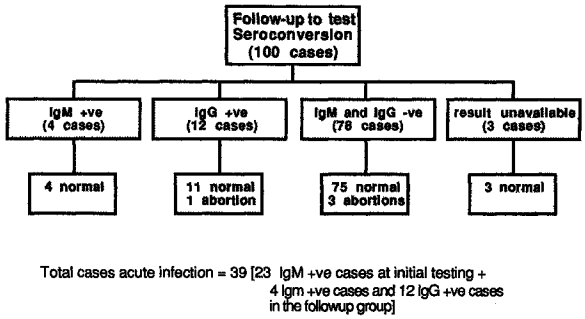

Fig. 1. An outline of patients included in the follow-up study.

in a primary health care center. Blood samples were obtained from 343, 406 and 298 cases in the first, second and third trimesters, respectively. To study the incidence of seroconversion, a second sample of blood was obtained 2–4 weeks later from the first 100 cases, who were IgG and IgM negative in the first trimester (Figure 1).

Acute infection was defined by the presence of IgM antibodies to parvovirus B19 at the first determination or by the development of IgG or/and IgM antibodies to parvovirus in previously seronegative women.

The symptoms checked for were fever, rash and arthritis alone or in combination.

Laboratory Methods

Human serum IgG and IgM antibodies to parvovirus B19 were detected by a high quality enzyme immunoassay (IDEIA, DAKO) which are developed to provide the optimal specificity and sensitivity of the assay system. This is obtained by: (1) use of non-infectious, empty viral capsid as antigen, produced in insect cells infected with recombinant baculovirus encoding for the capsid protein VP2, (2) use of u-capture technique for the detection of B19 specific IgM antibodies. The sensitivity and specificity of anti-B19 IgG assay are based on that of the golden standard, radioimmunoassay. The sensitivity of the assay is 98% while the specificity is 96%.[14]

Statistical Methods

The statistical method used was the Z-test of proportion and the chi-square test for association between categorical variables. The value of $P \leq 0.05$ was used as the cut-off level of significance.

RESULTS

The demographic features of the 1,047 patients included in the study are shown in Table 1. The mean maternal age and parity of the patients who were in the third trimester were significantly higher compared to patients who were in the first and second trimester ($P < 0.01$, $P < 0.0001$, respectively).

The overall prevalence for parvovirus B19 IgG positivity was 53.3% and IgM seropositivity was 2.2% at the initial testing. The result of parvovirus B19 IgG and IgM seropositivity is shown in Table 2. The prevalence of parvovirus B19 IgM seropositivity in the three trimesters did not show significant difference. However, IgG seropositivity was significantly higher in the first and second trimester (54.5 and 59.5%, respectively) compared to third trimester (47.6%) ($P < 0.01$, $P < 0.001$, respectively).

Parity and Parvovirus B19 IgG and IgM Seropositivity in Different Trimesters

The percentage of IgM positive cases with a parity of 5 or more is significantly higher in all three trimesters compared to mothers in the lower parity groups (Figure 2). IgG seroprevalence in the third trimester is significantly lower than first and second trimester in all parity groups (except parity of 5 or more) (Figure 3).

Age and Parvovirus B19 IgG and IgM Seropositivity in Different Trimesters

There was no statistically significant difference among the different age groups in terms of IgM seropositivity in different trimesters (Figure 4). Overall prevalence of IgG seropositivity was significantly affected by maternal age with the highest seropositivity in mothers with age groups ≤ 24 and 25–35 compared to mothers in age group of ≥ 36 irrespective of the trimesters. When we studied it in relation to trimester of pregnancy, the prevalence of IgG antibodies to parvovirus B19 in the age groups < 24 and 25–35 was still higher in first and second trimesters compared to third trimester ($P < 0.01$) (Figure 5).

Nationality and Parvovirus B19 IgG and IgM Seropositivity in Different Trimesters

IgG seropositivity was significantly higher in non-Kuwaiti mothers (58.5%) when compared to Ku-

TABLE 1. Distribution of maternal demographic features in the three trimesters

Maternal feature	1st trimester (343)	2nd trimester (406)	3rd trimester (298)	'P' value	Total (1047)
Age (mean ± SD)	26.92 ± 5.99	27.28 ± 5.06	28.38 ± 5.97	<0.01*	27.53 ± 5.66
Parity (mean ± SD)	1.25 ± 1.71	1.22 ± 1.5	2.13 ± 1.95	<0.0001*	1.55 ± 1.79
Nationality [N (%)]					
Kuwaiti	106 (29.2)	66 (18.2)	191 (52.6)	<0.0001#	363
Non-Kuwaiti	237 (39.9)	340 (49.7)	107 (15.6)		684

*P value by one-way ANOVA.
#P value by chi-square.

TABLE 2. Parvo B19 IgM and IgG seropositivity in the three trimesters

	IgM			IgG		
Trimester	(−ve)	(+ve)*	(E)	(−ve)	(+ve)#	(E)
1st	321 (93.6)	10 (2.9)	12 (3.5)	152 (44.3)	188 (54.8)	3 (0.9)
2nd	383 (94.3)	6 (1.5)	17 (4.2)	153 (37.7)	243 (59.8)	10 (2.5)
3rd	285 (95.6)	7 (2.3)	6 (2)	166 (55.7)	127 (42.6)	5 (1.7)

( )% *P value (P = NS) by chi-square.
#P value (P < .0001) by chi-square.

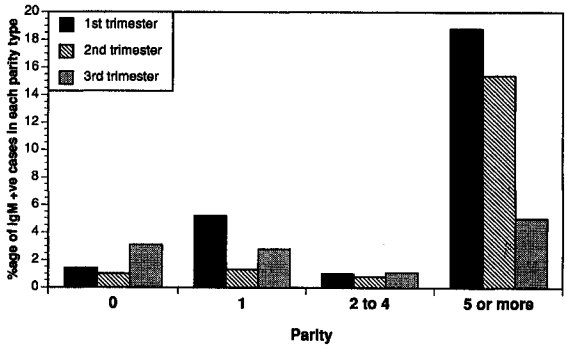

Fig. 2. Parvovirus B19 IgM seropositivity in relation to maternal parity and different trimesters.

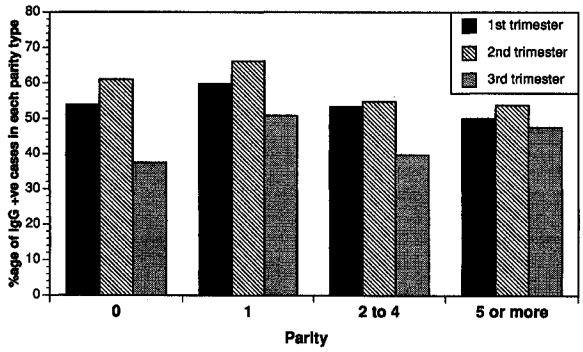

Fig. 3. Parvovirus B19 IgM seropositivity in relation to maternal parity and different trimesters.

waiti mothers (43.5%) ($P < 0.0001$). The distribution of IgG seropositive mothers in the three trimesters is shown in Figure 6. IgG seropositivity is significantly higher in Kuwaiti mothers in the third trimester ($P < 0.0001$) (Figure 6). IgM seropositivity was higher among Kuwaiti mothers (3.6%) compared to non-Kuwaiti mothers (1.5%) ($P < 0.05$). Distribution of IgM seropositive mothers in relation to nationality and trimesters is shown in Figure 7.

Logistic regression of IgG seropositivity as dependent variable and age, parity and trimester of pregnancy as independent variables selected the trimester of pregnancy as the only significant factor ($P < 0.05$). The same was done for IgM seropositivity and none of the factors were significantly related to the IgM seropositivity.

Acute Infection

Twenty three patients were parvovirus B19 IgM positive in the initial testing with their pregnancy outcome. Ten of these were in the first trimester, six in the second and seven in the third trimester. Four of the abortions occurred between 8–12 weeks and one of at 16 weeks of gestational age. Therefore, the abortion rate among the parvovirus B19 IgM positive group in the first and second trimester was 31.25%.

Among the 100 patients who were retested 2–4 weeks after an initial IgG and IgM negative result, 97 completed the two tests. Figure 1 shows the pregnancy outcome of these patients. The rate of parvovirus B19 acute infection between 9–14 weeks is 16.5%. The abortion rate in the first trimester in patients with acute infection was 19.2%

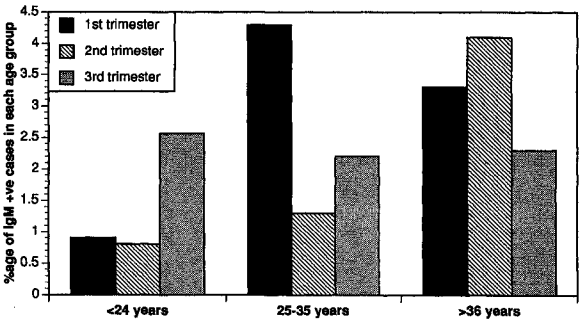

Fig. 4. Parvovirus B19 IgM seropositivity in relation to maternal parity and different trimesters.

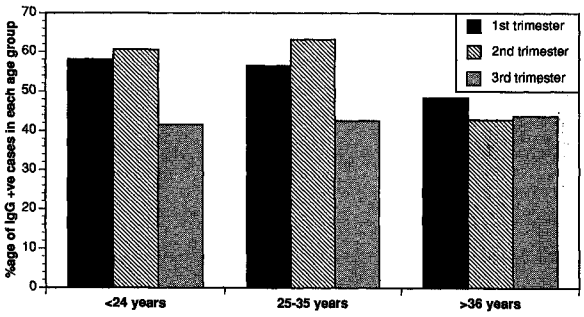

Fig. 5. Parvovirus B19 IgM seropositivity in relation to maternal parity and different trimesters.

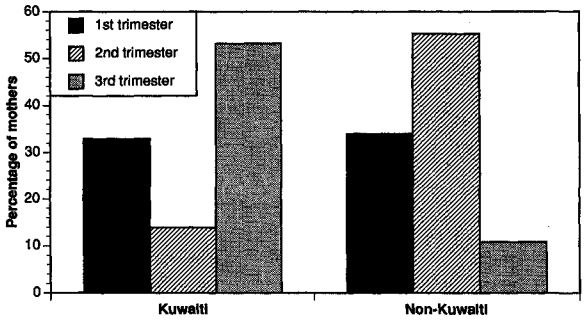

Fig. 6. Parvovirus B19 IgM seropositivity in relation to nationality of the mother and different trimesters.

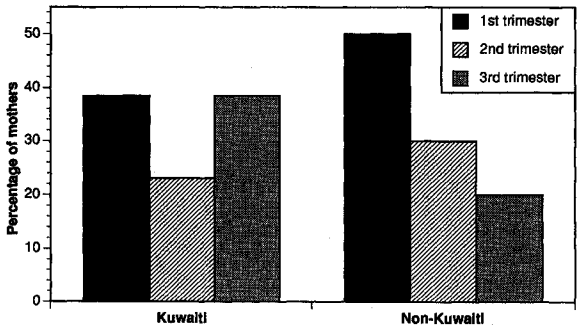

Fig. 7. Parvovirus B19 IgM seropositivity in relation to nationality of the mother and different trimesters.

compared to 3.7% who were seronegative between 9–14 weeks, and the difference is statistically significant ($P < 0.01$). Of the 32 who had acute infection in the first or second trimester, the abortion rate was 18.75%. In mothers with acute infection, the abortion rate was 14.3% in Kuwaiti and 16.7% in non-Kuwaiti mothers.

Symptom of Acute Infection

Only 17.9% mothers with acute infection were symptomatic and none of these mothers had fetal loss. Six of these symptomatic cases were in the first trimester. There was no significant difference in abortion rate among symptomatic IgM positive (0/6) and asympytomatic IgM positive mothers (5/20).

DISCUSSION

In most of the mothers with confirmed parvovirus B19 infection, the pregnancy outcome is favorable, whereas in others for reasons not well understood, adverse fetal outcome like miscarriages, hydrops fetalis and death may occur.

The fetus seems to be most susceptible to parvovirus B19 infection during the first and second trimester of pregnancy and especially between weeks 10 and 20[11] which coincide with the major development of the erythroid precursors. Parvovirus B19 has a propensity for infecting rapidly dividing cells, particularly erythroblasts. Between the third and sixth months of pregnancy the fetal red blood cell mass increases thirty times, with a risk of developing anemia if the fetus is infected by parvovirus virus B19[15]. By the third trimester, the fetus is able to mount a more effective immune response to the virus, which may account for the decrease in fetal loss at this stage of the pregnancy.

In a large prospective study, 186 women seroconverted during pregnancy. There were a total of 30 pregnancy losses, 7 of which occurred in the first 12 weeks of gestation, 20 during weeks 13–20, 1 between 21–27 weeks, 1 between 28–40 and one at an unknown time.[11] In another study, 134 IgM positive pregnant women were included. Of these, 46 were in the first 8 weeks of pregnancy. Fifteen percent of these resulted in pregnancy loss, 66 cases were between 10–18 weeks, out of which

there were 11 (17%) fetal deaths. Of the 13 women between 19–27 weeks, none had a fetal loss.[10] We found in the initial testing that there were a total of 5 fetal losses among the 23 IgM positive cases, 4 of which occurred 8–12 weeks of gestation and 1 occurred at 16 week of gestation. In the subsequent testing for seroconversion, there was one case of fetal loss which occurred at 12 weeks of gestation.

Incidence of fetal loss secondary to parvovirus B19 was initially estimated to be as high as 26–38%.[16–17] However, recently this loss is thought to be much lower, usually < 10%.[11,18,19] In our study group, the abortion rate in those patients who had acute infection was 15.4%. Although we detected antibodies to parvovirus B19 in women who aborted, we cannot state that parvovirus B19 was the cause, since we did not perform PCR for parvovirus B19 DNA and electron microscopy for viral particles. Therefore incidence of fetal loss secondary to Parvovirus B19 may be lower than we reported.

The incidence of acute infection during pregnancy is reported to be 1.5–3.7%.[18,20] Our seroconversion rate of 16.5% is much higher, which may be related to a number of epidemiological variables including climate.

The reported incidence of asymptomatic infection after parvovirus B19 infection is in the range of 20–53% in non-pregnant patients.[21,22] However, the incidence of asymptomatic infection in pregnant patients was shown to be higher reaching 70%.[18] Accordingly, the estimate of the incidence of parvovirus B19 infection in pregnancy on the basis of clinical symptoms may underestimate the true incidence of acute infection during pregnancy. In our group, the incidence of symptoms in acute infection group is even lower (17.9%). Previously it has been shown that pregnant women with asymptomatic parvovirus B19 infection are at a greater risk than those reporting symptoms.[13] Similarly in our study, of the patients with acute infection in the first trimester, 20% mothers with asymptomatic infection aborted, while none (0/6) of the mothers with symptoms aborted. However, the difference was not statistically significant.

Seroprevalence of IgG antibodies to parvovirus B19 increases with age. A survey in the USA showed a gradual increase in seropositivity with age ranging from as low as 19% in children under 10 years of age to 67% in individuals over 49 years of age, suggesting continuing exposure to the virus.[20] A Japanese study showed that the prevalence of human parvovirus B19 rose with increasing age, starting just above 10% in children under 10 years and reached more than 50% in subjects over 60 years.[23] Contrary to other reports our study showed the highest IgG parvovirus B19 seroprevalence among patients who were less than 36 years of age. The percentage of IgM seropositivity in grandmultiparas was higher compared to mothers with lower parity. It seems that nationality was a major factor affecting the prevalence of IgG antibodies and IgM. This might reflect the general effect of epidemiology of parvovirus B19 in the countries from which non-Kuwaiti population, in Kuwait, came from. The lower prevalence of IgG seropositivity among Kuwaiti put them at a higher risk of acquiring parvovirus B19 during pregnancy, especially in countries with large numbers of visitors and an epidemic could follow.

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