PREVALENCE OF ANTIBODIES TO HUMAN PARVOVIRUS B19 IN SAUDI WOMEN OF CHILDBEARING AGE IN MAKKAH

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INTRODUCTION
Parvovirus B19 is a single-stranded DNA-virus that was serendipitously discovered in the mid-1970s by Yvonne Crossart, a medical virologist, screening blood donors for hepatitis. During electrophoresis, an abnormal band was noted in sample number 19, panel B. Therefore, the virus was named "B19", and subsequently identified as a parvovirus. Parvovirus B19 infection, an acute self-limiting disease also known as the fifth disease or erythema infection, commonly occurs in children of primary school age. The typical rash ('slapped cheek' appearance) is immune mediated, since it coincides with the appearance of IgM and IgG specific antibodies.

The virus binds to its cellular receptor, the P-antigen, and has a tropism for immature erythrocytes in the bone marrow or fetal liver. Infection leads to an inhibition of erythropoiesis, resulting in anemia. Other tissues, such as the myocardium and endothelial cells, can also be affected. Clinical signs are usually fever and rash, arthralgia or such signs as febrile illness with malaise. The infection can also be...
asymptomatic. In pregnant women, the virus is known to be associated with fetal anemia, fetal hydrops, spontaneous abortion and intrauterine fetal death (IUFD). Several cases of IUFD caused by a combination of infection in the second or third trimester and hydrops are reported. Parvovirus B19 has also been demonstrated to be a significant cause of mid-trimester abortions.

However, most infections with parvovirus B19 remains asymptomatic, and therefore, the majority of exposed persons have no recollection of previous symptoms. The specific immunoglobin M (IgM) antibody detection has been the core diagnostic test for acute parvovirus B19 infection, while the appearance of immunoglobulin G (IgG) antibodies is indicative of previous exposure to the virus. The prevalence of seropositivity to parvovirus B19 infection in pregnant women, in Saudi Arabia, has not been previously described. The aim, therefore, of this study was to determine the seroprevalence of parvovirus B19 in the obstetric population in Makkah, Saudi Arabia, and to compare the results to those of other countries.

SUBJECTS AND METHODS
A total of 1200 randomly selected pregnant Saudi women in their first trimester attending the Maternity and Children's Hospital, Al-Noor Specialist Hospital, Hira General Hospital and King Abdul-Aziz General Hospital in Makkah city, for antenatal care were included in the study.

The study was carried out from November 2005 to October 2006. The age range of the patients was 16-45 years, with a mean age of 27 years. 10ml samples of blood were collected from each of the patients after informed consent. Serum was separated, aliquoted into two eppendorf tubes and stored at -20 °C until testing. Human serum IgG and IgM antibodies to parvovirus B19 were detected by enzyme-linked immunosorbent assay (ELISA) (EIA gen parvovirus B19 IgG kit, EIA gen parvovirus B19 IgM kit- Adaltis, Italia).

Ethical Consideration
An informed consent was obtained from each individual before inclusion in the study. Every subject had been informed about the procedure before the blood sample was collected, making absolutely certain that she understood the procedure to be carried out. These subjects were also made aware that they could refuse to participate in the study without prejudice.

RESULTS
Of the 1200 women who were tested for the presence of specific IgG antibodies 560 women (46.6%) tested positive for parvovirus B19 antibodies in the first trimester of pregnancy, implying immunity for parvovirus (Table 1). Twenty-seven (2.25%) women tested positive for IgM parvovirus B19 antibodies in the first trimester of pregnancy. The seroprevalence of IgG and IgM for parvovirus B19 specific IgG and IgM antibodies among different age groups increased with age: the lowest prevalence respectively (33.6%) (0.81%) was detected in women between 16-20 years of age reaching (53.9%) in those above the age of 36 for IgG antibodies and (3.92%) for IgM in women above the age of 40 (Table 2).

| No. of antenatal sera tested | No. of positive IgG (%) | No. of positive IgM (%) |
|-----------------------------|-------------------------|------------------------|
| 1200                        | 560 (46.6)              | 27 (2.25)              |

| Age groups | No. of positive IgG/No. tested (%) | No. of positive IgM/No. tested (%) |
|------------|-----------------------------------|-----------------------------------|
| 16-20      | 41/122 (33.6)                     | 1/122 (0.8)                       |
| 21-25      | 122/281 (43.4)                    | 5/281 (1.8)                       |
| 26-30      | 183/381 (48.0)                    | 7/381 (1.8)                       |
| 31-35      | 110/213 (51.6)                    | 7/213 (3.3)                       |
| 35-40      | 82/152 (53.9)                     | 5/152 (3.3)                       |
| 41-45      | 22/51 (43.1)                      | 2/51 (3.9)                        |

DISCUSSION
Infection with parvovirus is common worldwide. The yearly peak incidence of infection occurs in the spring and epidemics occur every 4 years. The prevalence of IgG antibodies directed against B19 in the population ranges from 2 to 15% in children 1-5 years old, 15-60% in children 6-19 years old, 30-60% in adults and more than 85% in the geriatric population. About 35-45% of women of childbearing age do not possess protective IgG antibodies against B19. The incidence of acute B19 infection in pregnancy is approximately 1-2% in endemic periods, but in epidemic periods the infection rate may rise to >10%.
The prevalence of parvovirus B19 infection in pregnant women, in Saudi Arabia and other countries in the Arabian Gulf (except Kuwait) has not been described previously. In Kuwait, England, USA, Spain and Japan, the prevalence was found to be 53.3, 53, 49.7, 35 and 33% respectively. In our study, seropositivity was found in 46.6%, which is similar to other studies. This is lower than the 81% reported in England, USA, Spain and Japan, the prevalence is frequently found in 46.6%, which is similar to other studies. Preventing the infection in pregnancy would be one possible application of the present candidate vaccine. Recently, Ballou et al (2003) described a recombinant parvovirus B19 vaccine composed of VP1 and VP2 capsid protein, which proved to be immunogenic and safe to use in human volunteers. Vaccination of non-immune pregnant women could be a highly effective method of preventing fetal infection with B19. However, the cost-effectiveness of this strategy in the general population is uncertain. This study may also suggest that there is a need to launch an awareness program for pregnant women. Additional studies of this nature should be encouraged to improve the knowledge of the Saudi population about the risks of exposure of pregnant women to parvovirus B19.

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REFERENCES
1. Young NS, Brown KE. Parvovirus B19. New Engl J Med 2004;350:586-97.
2. Brown KE, Anderson SM, Young NS. Erythrocyte P antigen: cellular receptor for B19 parvovirus. Science 1994; 262: 114-7.
3. Porter HJ, Quantrill AM, Flemin KA. B19 parvovirus infection of myocardial cells. Lancet 1988;1:535-6.
4. Public health laboratory service working party on fifth disease. BMJ 1990;300:1166-70.
5. Heegaard. ED, Hindsleh A. Parvovirus: the expanding spectrum of disease. Acta Pediatr 1995;84:109-17.
6. Jordan JA. Identification of Human Parvovirus B19 in idiopathic non-immune hydrops fetalis. Am J Obstet Gynecol 1996;174:37-42.
7. Morey AL, Keeling JW, Peter HJ, Fleming KA. Clinical and histopathological features of parvovirus B19 infection in the human fetus. Br J Obstet Gynecol 1992;56:74.
8. Forouzan I. Hydrops fetalis; recent advances. Obstet Gynecol Surv 1997;52: 130-8.
9. Sanghi A, Morgan-Capner P, Hesketh L, Elsleim M. Zoonotic and viral infection in fetal loss after 12 weeks. Br J Obstet Gynecol 1997;104:942-5.
10. Wright C, Hindcliffe SA, Taylor C. Fetal pathology in intrauterine death due to parvovirus B19 infection. Br Obstet Gynaecol 103:133-36.
11. Sabella C, Goid FJ. Parvovirus B19 infection. Am Fami Physicians 1999;60: 1455-60.
12. Brown KE, Young NS, Barbosa L. Parvovirus B19: implication for transfusion medicine. Summary of a workshop. Transfusion 2001;41:130-5.
13. Bosman A, Wallinga J, Kroes ACM. Fifth disease every four years: parvovirus B19. Infectieziekenbulletin 2002;6:215-9.
14. Heegaard ED, Brown KE. Human parvovirus B19. Clin Microbiol Rev 2002; 15:485-05.
15. Jon EP, De Haan TR, Kroes ACM Beersma MFC, et al. Parvovirus B19 infection in pregnancy. J Clin Virol 2006;7:1-7.
16. Dembinski J, Eis-Hubinger AM, Maar J, Schild R, Bartman P. Long term follow up of serostatus after materno fetal parvovirus B19 infection. Arch Dis Child 2003;88: 219-21.
17. Trotta M, Azzi A, Meli M, Borch B, Periti E, Pontello v, et al. Intrauterine parvovirus B19 infection: early prenatal diagnosis is possible. Int J Infect Dis 2004;8:130-1.
18. Valeur-Jensen AK, Pedersen CB, Westergaard T, et al. Risk factors for parvovirus B19 infection in pregnancy. JAMA 1999;1099-1105.
19. Maksheed M, Paca SA, Essa SS, et al. The prevalence of antibody to human parvovirus B19 in pregnant women in Kuwait. Acta Tropi 1999;73: 225-9.
20. Cohen BJ, Bukley MM. The prevalence of antibody to human parvovirus B19 in England and Wales. J Med Microbiol 1988;25: 151-3.
21. Harger JH, Adler ST, Koch WC, Harger FF. Prospective evaluation of 618 pregnant women exposed to parvovirus B19: Risk and Symptoms. Obstet & Gynaecol 1998;91:413-20.
22. Grecatos E. The incidence of human parvovirus B19 infection during pregnancy and its impact on preinatal outcome. J Infect Dis 1995;171:1360-3.
23. Yaegashi N, Okamura K, Hamazaki Y, et al. Prevalence of anti-human parvovirus antibody in pregnant women. Nippon Sanka Fujinka Gakki Zasshi 1999;42:162-6.
24. Sparre LS, Fridell E, Nyman M, et al. A prospective study antibodies against B19 in pregnancy. Act Obstet Gynecol Scand 1996;75:336-9.
25. Cohen BJ, Kumar S. Parvovirus B19 infection in pregnancy. Fetal Mater Medc Rev 2005;16:123-50.
26. Ballou WR, Reed JL, Nible W, et al. Safety and immunogenicity of a recombinant parvovirus B19 vaccine formulated with MF59.C.i. J Inf Dis 2003; 187:675-8.