

# Age-Related Immunoglobulin G Seroprevalence of Human Parvovirus B-19 in Israeli Children

Dan Miron MD<sup>1</sup>, Yoseph Horovitz MD<sup>1</sup>, Anthony Luder MD<sup>2</sup>, Frederic S. Ohnona MsC<sup>3</sup> and Yechiel Schelisinger MD<sup>3</sup>

<sup>1</sup>Department of Pediatrics A, HaEmek Medical Center, Afula and <sup>2</sup>Department of Pediatrics, Ziv Medical Center, Safed, affiliated with Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel

<sup>3</sup>Infectious Disease Unit, Shaare Zedek Medical Center, affiliated to Hadassah-Hebrew University Medical School, Jerusalem, Israel

**ABSTRACT:** **Background:** Human parvovirus B19 is a global and common infectious pathogen in humans, particularly in children. **Objectives:** To assess the immunoglobulin G seroprevalence of B19 in children in Israel. **Methods:** Overall, 128 previously healthy children (1.5–17 years old) hospitalized for various diseases other than acute human parvovirus B19 infection were assessed for IgG to the virus by enzyme-linked immunosorbent assay. **Results:** The IgG seroprevalence increased from 22% in children aged 1.5–9 years to 52% in older children ( $P = 0.001$ ). **Conclusions:** Our data suggest that most acute parvovirus B19 infections in Israel occur in the early school years, and that by 18 years of age 50% of Israeli children have been infected by the virus.

IMAJ 2010; 12: 277–279

**KEY WORDS:** parvovirus B19, immunoglobulin G, seroprevalence, child

**H**uman parvovirus B19, a member of the family Parvoviridae, is a global and common infectious pathogen in humans, primarily in children [1]. In previously healthy children, symptomatic B19 infection has been associated with several clinical syndromes, such as various exanthema diseases, acute arthropathies, and acute hematologic manifestations including transient aplastic crisis or pancytopenia. Additionally, B19 infection of patients with chronic hemolytic diseases may be associated with severe aplastic crisis. In many children, the infection may be either asymptomatic or non-typical [1–3], but they may transmit the infection to susceptible children and adults including pregnant women. Acute B19 infection occurs in 1–5% women during pregnancy, and the prevalence increases to 3–20% during epidemics. Although transplacental fetus infection occurs in about 30–50% of

acutely infected pregnant women, most fetuses develop normally. However, maternal infection during the first 20 weeks of pregnancy may be associated with severe anemia, non-immune hydrops fetalis and fetal loss in up to 9% if undiagnosed and untreated [1,10]. Data on B19 epidemiology in Israeli children are lacking.

The aims of the current study were to assess the IgG seroprevalence of B19 among healthy children in Israel, and evaluate the possible susceptibility for B19 infection among women of childbearing age.

## PATIENTS AND METHODS

This study is a continuum of a recently published study evaluating the role of B19 infection in Israeli children aged 1.5–17 years hospitalized with various clinical syndromes compatible with acute B19 infection. The study was prospective and ran from 1 October 2002 to 30 August 2004 in three pediatric departments in Israel – HaEmek Medical Center in Afula, Sieff Medical Center in Safed, and Shaare Zedek Medical Center in Jerusalem. Institutional review boards in these hospitals approved the study and informed consent was obtained from parents before inclusion.

The study group comprised 167 children, whose mean age was  $5.5 \pm 4.6$  (range 0.5–17) years. Each enrolled child had a serum specimen tested for the presence of parvovirus B19 DNA by real-time polymerase chain reaction and for the presence of anti-parvovirus B19 IgM and IgG antibodies, tested by enzyme-linked immunosorbent assay [3,4]. By definition, a hospitalized child with compatible symptoms who had either B19 DNA by real-time PCR, or anti-parvovirus IgM, was considered as having acute B19 disease.

Of the 167 hospitalized children (age 1–17 years) in the study, 128 were found not to have acute B19 disease. Analysis of the IgG seroprevalence in this latter group constitutes the current study.

Data analysis was performed using the SPSS statistical

IgG = immunoglobulin G  
B19 = human parvovirus B19

PCA = polymerase chain reaction

**Table 1.** Age-related parvovirus IgG seroprevalence in Israeli children

Age (yrs)	1.5–5	6–9	10–15	16–17
Overall	54	43	23	8
IgG positive PCR and IgM negative	11	10	12	4
%	20.4%	23.2%	52%	50%

package. Prevalence rates of B19 IgG seroprevalence were compared by chi-square test. *P* values were two-sided, with a significance level of *P* < 0.05.

## RESULTS

The 128 children who fulfilled the inclusion criteria of this study were equally distributed between males and females. IgG seroprevalence in these children is shown in Table 1. The overall B19 IgG seroprevalence increased from 21.6% (21/97) in children 1.5–9 years old to 51.6% (16/31) in older children (*P* = 0.001 by chi-square test). No significant differences in seroprevalence rates were documented among age groups of children between boys and girls.

## DISCUSSION

The present study, the first in Israel to assess age-related B19 IgG seroprevalence in children, shows that by 18 years of age about 50% of Israeli children have been infected by B19. Our results are concordant with recently published data from other countries, mostly European, showing that the percentage of people with measurable levels of B19-specific IgG

increases with age from 5–40% at age 1–9 years to 40–63% at age 10–18 years, with most individuals becoming infected during their school years [Table 2]. Vyse et al. [8] showed that B19-specific IgG prevalence rose non-linearly with age from 21% in those aged 1–4 years to > 75% in adults aged ≥ 45 years. Force-of-infection estimates were similar to those made in 1991, the highest being in those aged < 15 years. There was no association between evidence of previous infection and gender or region. This phenomenon can be explained by the combination of two factors: namely, the mode of transmission of the virus in the community and the relatively high prevalence of the disease in childhood.

B19 is transmitted primarily through respiratory secretions and saliva. Therefore, in crowded environments such as daycare centers, kindergartens and schools, transmission of the virus from infected to non-infected individuals is probable [1].

The most typical disease associated with B19 in children is erythema infectiosum, which is clinically easy to diagnose and peaks at age 7–9 years. However, acute B19 infection may also be sub-clinical or presents with other non-specific manifestations associated with the virus. Barash and co-authors [2] described the clinical presentation of 40 children hospitalized with acute B19 infection as diagnosed by the presence of B19 IgM. They found that prolonged, recurrent or intermittent fever appeared in two-thirds of the children of whom most were over 4 years of age, and it was accompanied by a rash in only a few. Other manifestations included arthropathy and unexplained non-responding anemia. In our prospective original study we detected acute B19 disease in 21 of 149 children (12.6%) of whom 10 presented with a variety of acute exanthema diseases (none had typical erythema infectiosum); 5 presented with acute arthropathy (all 5 had transient synovitis), 4 presented with transient pancytopenia or aplastic anemia, and 2 children presented with fever of > 1 week [3]. Tuckerman and collaborators [9] described an outbreak of erythema infectiosum in a village primary school, where the course of disease in 14 of 64 children and adults (22%) with serologically proven recent B19 infection was sub-clinical.

We are not aware of any study in Israel assessing B19 seroprevalence among adults. Studies conducted in Europe show a prevalence of 30–60% in adults and more than 85% in the geriatric population. As shown in Table 2, in countries with a B19 seroprevalence rate among children similar to that of Israel, 30–40% of women aged 18–19 years are susceptible to B19 infection. Parvovirus infection during pregnancy can cause severe fetal anemia as a result of fetal erythroid progenitor cell infection with a shortened half-life of erythrocytes, causing high output cardiac failure and subsequently non-immune hydrops fetalis [1,10]. If data in Israel are concordant with those of Europe, and assuming 0.6–3% primary infection during the first two trimesters of pregnancy and 150,000 pregnancies/year in Israel based on

**Table 2.** Results of recent published surveys of IgG B19 seroprevalence in various countries

Author [ref], yr	Year of survey	No. of children studied	Country	1–9 yrs	10–18 yrs	Susceptible at 18–19 yrs**
Kelly et al. [5], 2000	1992-8	202	Victoria, Australia	28%	51%	33%
Mossong et al. [7], 2008	1996	NA	England & Wales	22–33%	60–63%	38%
Mossong et al. [7], 2008	1997-8	NA	Finland	5–30%	30–50%	49%
Mossong et al. [7], 2008	2003-4	NA	Italy	10–40%	40–60%	40%
Mossong et al. [7], 2008	1995-2004	NA	Poland	20–40%	40–60%	40%
Vyse et al. [8], 2008	1997-8	426	Germany	40%	55%	33%
Current study	2004	128	Israel	22%	52%	NA

\*Rounded numbers

\*\* Susceptible to acute B19 infection

NA = not available,

available data, it is estimated that potentially about 900–4800 pregnant women might be infected with B19, resulting in up to 50% (450–2400) infected fetuses and a possible fetal loss of up to 9% (40–215) per year. It has been shown that early detection and diagnosis of the infection and fetal anemia by amniocentesis and/or cordocentesis leading to repeated transfusion of erythrocytes to the fetus may lower the mortality rate associated with non-immune hydrops fetalis from 50 to 18% [10]. Since data regarding B19 IgG seroprevalence among childbearing women in Israel are lacking, a prospective study assessing this issue as well as the prevalence of B19-associated non-immune hydrops fetalis is needed in order to plan a national preventive approach.

In conclusion, B19 infection is frequent in children in Israel and by 18 years of age about 50% of children have been infected, suggesting a relatively high susceptibility to B19 infection among young pregnant women.

---

**Correspondence:****Dr. D. Miron**

Dept. of Pediatrics A, HaEmek Medical Center, Afula 18101, Israel

**Phone/Fax:** (972-4) 649-5248**email:** miron\_da@cclalit.org.il**References**

1. Heegaard ED, Brown KE. Human parvovirus B19. *Clin Microbiol Rev* 2002; 15: 485-505.
2. Barash J, Dushnitsky D, Shoenberger D, Bardenstein R, Barak Y. Human parvovirus B19 infection in children: uncommon clinical presentations. *IMAJ* 2002; 4: 763-5.
3. Miron D, Luder A, Horovitz Y, et al. Acute human parvovirus B-19 infection in hospitalized children: a serologic and molecular survey. *Pediatr Infect Dis J* 2006; 25: 898-901.
4. Aberham C, Pendl C, Gross P, Zerlauth G, Gessner M. A quantitative internally controlled real time-PCR assay for the detection of parvovirus B19 DNA. *J Virol Methods* 2001; 92: 183-91.
5. Kelly HA, Siebert D, Hammond R, Leydon J, Kiely P, Maskill W. The age-specific prevalence of human parvovirus immunity in Victoria, Australia compared with other parts of the world. *Epidemiol Infect* 2000; 124(3): 449-57.
6. Röhrer C, Gärtner B, Sauerbrei A, et al. Seroprevalence of parvovirus B19 in the German population. *Epidemiol Infect* 2008; 136: 1564-75.
7. Mossong J, Hens N, Friederichs V, et al. Parvovirus B19 infection in five European countries: seroepidemiology, force of infection and maternal risk of infection. *Epidemiol Infect* 2008; 136: 1059-68.
8. Vyse AJ, Andrews NJ, Hesketh LM, Pebody R. The burden of parvovirus B19 infection in women of childbearing age in England and Wales. *Epidemiol Infect* 2007; 135(8): 1354-62.
9. Tuckerman JG, Thomas Brown T, Cohen BJ. Erythema infectiosum in a village primary school: clinical and virological studies. *R Coll Gen Pract* 1986; 36: 267-70.
10. Ergaz Z, Ornoy A. Parvovirus B19 in pregnancy. *Reprod Toxicol* 2006; 21: 421-35.