

## Seroepidemiology of Human Parvovirus B19 in 5-25 Year Old Age People in Iran

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### Abstract

**Background:** Parvovirus B19 (B19) is the only member of the family Parvoviridae associated with human infection. Although there are some studies to estimate the immunity to parvovirus in various populations but there is no seroepidemiological survey from Iran until now thus the age-specific immunity to human parvovirus infection was estimated.

**Methods:** A subset sample of 1500 study subjects in 2004 after Measles and Rubella mass campaign was selected from the original samples of 5000 sera kept at the Department of Virology in Tehran University of Medical Sciences. All sera were tested by a commercial ELISA kit.

**Results:** Totally, 1303 (86.6%) of 1500 study subjects were seropositive for B19 IgG antibody. The seropositive rate of males and females were 85.3% and 88%, respectively ( $P= 0.129$ ). The overall B19 seropositive rates in rural and urban were 84.3% and 88%, respectively ( $P= 0.044$ ). The seropositive rates were found to increase significantly with age and ranged from 79.3% in 5-9 year old group to 93.5% in 20-25 yr old group ( $P= 0.000$ ).

**Conclusion:** Our results indicate that in spite of high prevalence of B19 antibody the importance of routine diagnosis of B19 infection in order to elucidate the etiology of some unexplained 'exanthemata diseases' especially in measles elimination and eradication phase is needed.

**Keywords:** Human parvovirus B19, ELISA, Seroepidemiology, Iran

### Introduction

Parvovirus B19 (B19) is the only member of the family Parvoviridae associated with human infection. B19 is a small DNA virus with single-stranded, linear genomes approximately 5 kb in length (1, 2). The virus is responsible for various clinical manifestations whose characteristics depend on the interplay between the viral properties and the physiological and immune status of the infected individuals (3). Parvovirus B19 infection is global. It is common in childhood, continues at a low rate throughout adult life, and by the time they are elderly, most people are sero-positive (4). IgG antibodies to parvovirus B19 can be detected in serum 2-3 wk after acquisition of infection and last for life, providing immunity against re-infection (5). Transmis-

sion of infection occurs via the respiratory route, through blood-derived products administered parenterally and vertically from mother to fetus (6). The spectrum of disease linked to human parvovirus B19 is the cause of the childhood disease erythema infectiosum or fifth disease (7). The peak incidence of erythema infectiosum is in late winter and early spring (8). Dermal affection is less frequent and uncharacteristic in the adult population (9). In contrast, arthralgia and arthritis are the most common manifestations of primary B19 infection in adults particularly in adult females (10).

Parvovirus B19 may cause transient anemia amongst healthy adults, aplastic crises in infected persons with an underlying blood disorder (11) prolonged anemia in immuno-compromised persons

(11, 12). In addition parvovirus can cause hydrops fetalis and fetal death if a pregnant woman becomes infected during the pregnancy (13). Estimates of population susceptibility to human parvovirus are useful in assessing the risk to erythema infectiosum (fifth disease) pregnant women (14), because primary prevention is not feasible as no vaccines against parvovirus B19 infection are currently approved (15). In the other hand the lack of the typical rash pattern in a large proportion of parvovirus B19 and the similarity of clinical manifestations to other rash diseases, especially to rubella, highlight the difficulty of diagnosing B19 infection on clinical grounds alone. Moreover, parvovirus B19 infection shares the seasonal pattern with rubella and measles, i.e., late winter and spring, which makes clinical diagnosis even more difficult especially in measles elimination and eradication phase (16). Therefore it is important to know about immune status of people against this virus.

This study provides an estimate of immunity to infection with parvovirus in 5-25 yr old healthy people in Iran.

## Materials and Methods

A subset sample of 1500 study subjects, ranging from 5 and 25 yr of ages, was selected from the original samples of 5000 sera kept at the Department of Virology in School of public Health, Tehran University of Medical Sciences, Iran. The original samples had been collected by multi-stage sampling in 2004 after Measles and Rubella mass campaign for evaluation of measles and rubella immunity from whole of the country. The country divided into high, medium and low risk districts strata according to measles epidemiology. Clusters were selected in each stratum proportionally to the size of low, medium and high risk strata and study subjects were recruited sequentially among clusters. The Serum samples were collected from subjects after obtaining informed consent. A standardized interview with a structured questionnaire was used to obtain information regarding age, sex, place of residence (Urban/Rural) and district.

The serum samples were tested for the presence of anti B19 IgG virus antibody was carried out by commercially available ELISA Kits (Parvovirus B19 IgG antibodies, IBL, Hamburg, Germany) according to the manufacturer's instructions. In brief, sera were diluted (diluent buffer, 1/101) and incubated for 60 min at 37° C on a specific antigen precoated 96 well plate. After washing, peroxidase conjugated anti-human IgG was used as second antibody (incubation 30 min, 37° C). Tetramethylbenzidine (TMB) was added after an additional washing and incubated for 10 min at room temperature in the dark. The reaction was stopped with 1 M H<sub>2</sub>SO<sub>4</sub> after 15 min and the samples were measured using a Spectra Max microplate reader (Molecular Devices, Munchen, Germany) at 450 nm wavelength. Sample values were calculated from the standard curve using the mean OD. All samples, standards and the positive control were analysed as duplicates. A titer of >3.5 was considered positive.

## Statistical analyses

Statistical analyses were performed using SPSS Software version 11.5. Categorical data were analyzed using Fisher's exact test and the chi-square test with the continuity correction. All comparisons were two-sided and a *P* value less than or equal to 0.05 was considered as significant.

## Results

One thousand and three hundred three (86.9%) of the 1500 study subjects were seropositive for B19 IgG antibody. In other words, 13.1% of female subjects were susceptible to acquiring parvovirus B19 infection. The seropositive rate of males and females were 85.3% (560/656) and 88% (743/844), respectively (Table 1). There were no significant differences in the prevalence of immunity by sex. The overall B19 seropositive rates in rural and urban were 84.3% and 88%, respectively (*P*= 0.044). The seropositive rate in urban remained significantly higher than that of rural (*P*< 0.05). The seropositive rates were found to increase significantly with age and ranged from 79.3% in 5-9 yr old group to 93.5% in 20-25 yr old group (*P* trend=0.00) (Table 1). As

shown in Table 2, age and residential area remained significantly associated with seropositivity of B19 antibody. As demonstrated in Table 2 in age groups 5-9 and 10-14 in both in female and male rural residents had a significantly lower seropositive rate than urban residence (Table 2). Our result shows that the seroprevalence of parvovirus B19 in the women of childbearing age (15-19 and 20-25 yr) was 90.9% and 93.8% respectively (Fig.1).

**Table 1:** Associations with Seropositivity of Antibody against Hum a Parvovirus B19 for Demographic Characteristics in Iran

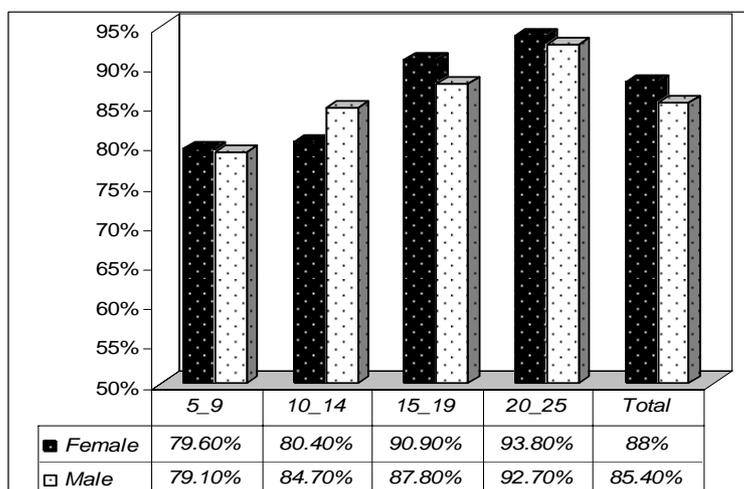
Variable	Group	no. Tested	no. Positive (%)	P
Sex	Male	656	560 (85.4)	0.129
	Female	844	743 (88.0)	
Residence	Rural	492	415 (84.3)	0.044
	Urban	1008	888 (88.1)	
Age (year)	5-9	329	261 (79.3)	0.000*
	10-14	362	300 (82.8)	
	15-19	378	339 (89.6)	
	20-25	431	403 (93.5)	

\* P for trend

**Table 2:** The prevalence of immunity to human parvovirus B19 by Place of residence , sex and 5 year age group .

Age group (years)	Place of residence	Females	Percent immune	Males	Percent immune	All subject	Percent immune
5-9	Rural	30	65.2	41	74.5	71	70.3
	Urban	91	85.8	99	81.1	190	83.3
10-14	Rural	37	75.5	61	82.4	98	79.7
	Urban	86	82.7	116	85.9	202	84.5
15-19	Rural	76	88.4	44	89.8	120	88.9
	Urban	134	92.4	85	86.7	219	90.1
20-25	Rural	87	94.6	39	95.1	126	94.7
	Urban	202	93.5	75	91.5	277	93
Total	Rural	230	84.2	185	84.5	415	84.3
	Urban	513	89.8	375	85.8	888	88.1

**Fig. 1:** Seroprevalence of IgG antibodies to B19 in Female and Male by age groups



## Discussion

B19 infection has been reported in many countries around the world. The seropositive rate of B19 IgG antibody varies by location (17). Parvovirus appears to be ubiquitous, common, and highly contagious and primarily is transmitted via the respiratory route (18). Although there is some

study to estimate the immunity to parvovirus in various populations in Iran but there is no sero-epidemiological survey from the whole country until now thus the age-specific immunity to human parvovirus infection was estimated. Most published studies have used samples of convenience to estimate the immunity to parvovirus in

various populations. The samples in this study were chosen to give an estimate of immunity in 5-25 yr age group who were at risk of measles before MR huge mass campaign in 2003 in Iran and are likely to represent population immunity in young age group. Sera of subjects were collected in 2004. The sera stored at the national measles laboratory and after 18 months were tested. In this study the seropositive rate in urban remained significantly higher than that of rural ( $P < 0.05$ ). The higher prevalence rate may have been because of the crowdedness of the population in the urban areas, because human parvovirus B19 is transmitted effectively after close contact exposure. This result might be attributed to the possible mode of B19 transmission by aerosol via the respiratory tract (17). In other study the seroprevalence rates in urban were reported higher at every age group. Thus, a densely populated city, and shows high seroprevalence rates (19). Many studies of the epidemiology of parvovirus have concentrated on women because of the risk to the fetus (18, 20, 21). A higher prevalence of parvovirus immunity amongst women might be expected because of their domestic, occupational exposure and depend on country of residence (22). On the other hand there are published reports of a higher apparent immunity amongst women (17, 23). A study in Tehran City in Iran showed that 80% and 93% of less than 14 old and 15-45 yr old women respectively were B19 IgG antibody positive (24). In Eritrea the pattern of antibodies to B19 showed a higher seroprevalence in all groups (56-91%) (25). In England, and Kuwait the prevalence of antibody to human parvovirus B19 in pregnant women was found to be 53% and 53.3% respectively (4, 26). However countries such as Taiwan (27), Hong Kong (28), Singapore (29), South Africa (30), Japan (31) and Spain (32) appear to have a different pattern of infection, resulting in population immunity among women aged 20-45 yr of approximately 25-35%. In Australia, prevalence of immunity amongst pregnant women was reported 50-60% (33). Our result shows that the seroprevalence of parvovirus B19 in the women

of childbearing age are higher than 90%. The finding that less than 9% women of childbearing age were susceptible to acquiring parvovirus B19 infection has important public health implications. Therefore the risk of parvovirus B19 infection in young woman in Iran is less than other country (27- 33).

Parvovirus is primarily a disease of childhood and, in a community outbreak, the highest attack rate is amongst children of school age (33). The association of parvovirus B19 seropositivity with age is consistent with population-based studies in the world (4, 8, 25, 34). Because, for parvovirus B19, seropositivity is a synonym of immunity, the increase of seroprevalence with age means that the proportion of individuals susceptible to parvovirus B19 decreases with age (34). The prevalence of antibodies to parvovirus B19 in adults is about 50% in the United States and Japan (7, 30) and 60-70% in England and Wales (4, 8). In Brazil and Niger a higher prevalence has been found with more than 80% of the children parvovirus B19 antibody positive at 10 yr of age (16, 35). It is estimated that, in the western world, by 15 yr of age 50% of all individuals have been infected, and these figures could rise to 80% or 100% in the elderly (36). In our study seropositivity was found in 86.9%, which is similar to other studies. For example this is 81% that reported in one area of Sweden during the years 1990-1991 (37).

As observed in Table 1 there was significant difference in IgG seropositivity in different age groups. The seropositive rates were found to increase with age and ranged from 79.3% in 5-9 yr old group to 93.5% in 20-25 yr old group in Iran. This is a high prevalence and indicates that transmission may occur earlier in life in Iran than in developed countries. Our results suggest that parvovirus B19 is common in Iran and support the view that parvovirus B19 virus has a worldwide distribution. A survey in the USA showed a gradual increase in seropositivity with age ranging from as low as 19% in children under 10 yr of age to 67% in individuals over 49 yr of age, suggesting continuing exposure to the virus (38).

Differences in population immunity between countries may be due to the sensitivity of the kits used and intensity of population. Some of Commercial assays which use a peptide are less suitable for seroprevalence studies than assays which use recombinant proteins (18). Other laboratories have also found problems with some of the commercial assays (39). B19 IgG test needs to be performed in diagnostic laboratories by ELISA assays using conformational B19 antigens (40). The importance of NS1 conformational epitope has been confirmed by Heegaard et al. who also observed a higher seroprevalence of IgG directed against the NS1 antigen by using native NS-1 in ELISA (78%) compared to Western blotting (33%) (41). The study confirmed that anti-NS1 IgG was present in 60% of patients recently infected by Parvovirus B19, thus suggesting that this novel test may be useful in cases where the VP2 ELISA test gave borderline results (39).

Many of studies indicated that the prevalence of IgG antibodies in females was higher than in males: Japan (female, 25.5%; male, 20.6%); USA (female, 51%; male, 38%); Germany (female, 48%; male, 32%); Brazil (female, 48.9%; male, 39.8%) (38, 42-44). This situation may reflect the more frequent close contact of women with children. Our results indicating no difference in the prevalence of IgG antibodies between males and females ( $P=0.129$ ). This result is similar to those observed in Rio de Janeiro (35) and Mexico (45). There was no difference in the prevalence of immunity by sex at any age group. Primary prevention is not feasible as no vaccines against parvovirus B19 infection are currently approved (46). Therefore it is important to know about immune status of people against this virus. Management options, however, are very limited as antiviral drugs are not available for the treatment of parvovirus B19 infection (46).

On December 2003, a mass campaign for measles/rubella vaccination was carried out in Iran during a rather huge plan, and more than 33 million dose of vaccine were administered to the 5 to 25 yr old populations. After mass campaign several infectious cause rash-fever disease that is commonly

mistaken for measles and Rubella. The introduction of test for roseolla (HHV6), dengue, Parvovirus B19 etc, into network laboratories will increase the need for identification of the cause of illness by public health teams and individual clinicians to avoid unnecessary public intervention (47). Therefore in spite of high prevalence of B19 antibody the importance of routine diagnosis of B19 infection in order to elucidate the etiology of some unexplained 'exanthemata diseases' especially in measles elimination and eradication phase is needed.

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