

Seroepidemiology of Human Parvovirus B19 among Pregnant Women in Erbil, Iraq

Nabaz Ahga, Kawthar Alharmni¹, Zakarea Alkhayat²

Department of Prevention Health, Erbil Medical Technical Institute, Erbil Polytechnic University, Departments of ¹Anatomy and Histology and ²Microbiology, College of Medicine, Hawler Medical University, Erbil, Iraq

Abstract

Background: Human parvovirus B19 (HPV B19) is a member of the family *Parvoviridae*. It can be transmitted congenitally from an infected mother to the embryo. The virus has been implicated in hydrops fetalis, spontaneous abortion, aplastic crisis, and acute symmetric polyarthropathy. **Objective:** The present study was carried out to determine the seroprevalence of HPV B19 immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies among apparently healthy pregnant women and to define the risk factors associated with. **Materials and Methods:** Blood samples were collected from consenting pregnant women who were attending Erbil Maternity hospitals from the period between January 2018 and June 2019. The sera were obtained from samples were analyzed for IgG and IgM antibodies of HPV B19 using (EUROIMMUN AG, Luebeck Germany) ELISA Classic Parvovirus B19 IgG/IgM kits. Structured questionnaire was used to obtain data on sociodemography and risk factors. **Results:** A total of 349 pregnant women were enrolled in this study and were screened for both IgM and IgG antibodies. Overall, 139 (39.8%) were positive for parvovirus B19 IgG and 32 (9.2%) had IgM antibody. Demographics including age group, occupation, number of children, and trimester of pregnancy. The differences of distribution of the Parvovirus IgG in relation to the above-mentioned demography were as follows: age >35 years: highly significant ($P \leq 0.01$), second trimester: nonsignificant, homemakers: highly significant ($P \leq 0.01$), ≥ 5 children highly significant ($P \geq 0.01$). The differences of distribution of the Parvovirus IgM in relation to the above-mentioned demography were as follows: age <20 years: significant ($P \leq 0.05$), second trimester: nonsignificant, homemakers: highly significant ($P \leq 0.01$), ≥ 5 children: significant ($P \geq 0.05$). **Conclusions:** HPV B19 is prevalent in Erbil, Iraq. More than half (51%) of the women were IgG negative, so they are susceptible to the HPV B19 infection. Hence, there is a need for routine screening for B19 IgM antibodies for all women of childbearing age and subsequent clinical management of positive cases.

Keywords: Human parvovirus B19, pregnant women, seroprevalence

INTRODUCTION

Human parvovirus B19 (HPV B19) belongs to the parvovirus genus of the family *Parvoviridae*, which constitutes the smallest and the simplest of the known DNA viruses.^[1] It has a diameter of 23 nm and comprises a single-stranded DNA genome (5.5 kb). The viruses in the parvo-virus genus are species specific and thus human parvovirus B 19 is the only recognized pathogenic parvovirus in humans.^[2] HPV B19 causes a number of clinical maladies including infectious erythema (fifth disease), hydrops fetalis, transient aplastic crises, arthropathy, and congenital aplasia.^[3] Transmission of infection takes place by means of respiratory route and blood-derived products administered parenterally and vertically from mother to fetus.^[4] Assessment of population predisposition to human parvovirus is useful in considering

the risk to pregnant women, because primary prevention is not feasible as no vaccines against parvovirus B19 infection are currently approved.^[5] On the other hand, the dearth of the exemplary rash pattern in a large portion of patients infected with parvovirus B19 and the resemblance of clinical manifestations to other rash diseases, especially to rubella highlight the difficulty of diagnosing B19 infection clinically alone.^[6] In general, diagnosis of parvovirus is based on clinical

Address for correspondence: Dr. Zakarea Alkhayat,
Department of Microbiology, College of Medicine,
Hawler Medical University, Erbil, Iraq.
E-mail: dr_zakarea@yahoo.co.uk

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symptoms and serologic antibody testing for parvovirus immunoglobulin G (IgG) and parvovirus immunoglobulin M (IgM).^[1,3] Past infection can be assured by the presence of IgG antibodies. Acute infection is revealed by the existence of IgM antibodies.^[4,5] The seroprevalence of HPV B19 appears to be variable worldwide.^[2] Various factors are recognized to impact seroprevalence including age, geography, climate, socioeconomic status, occupation, race, parity, and working among children.^[4]

This study was an attempt to investigate the prevalence and incidence of Human Parvovirus 19 IgG and IgM, respectively, with a possible relation with different demographic factors in a sample of apparently healthy pregnant Iraqi women in Erbil city, Iraq.

MATERIALS AND METHODS

Study protocol

This was a cross-sectional study which was performed from the period between January 2018 and June 2019. The study population included pregnant women attending the antenatal clinics in Erbil Maternity hospitals in Erbil city.

Ethical considerations

This study was approved by the Ethics Committee of Erbil Medical Technical Institute, Erbil Polytechnic University, Iraq, Health Directorate of Erbil, and College of Medicine Hawler Medical University. Informed consent was obtained from each woman in addition to their husbands or relatives before inclusion in the study. Before the blood sample was collected, the procedure was thoroughly explained to every person to ensure that they understood exactly what was going to happen. It was also pointed out to the individuals that they could refuse to participate in the study without prejudice.

Study population

Apparently healthy pregnant women with no previous history of abortion were selected by simple random method, ranging in age from 18 to 41 years and at various trimesters of pregnancy were included in this study. All pregnant women whose gestation ages were unknown and who had transfused with blood were excluded from the study. Before sample collection, clinical information, demographic information, and data on possible risk factors were collected from the women using structured questionnaires.

Analytical methods

Five milliliters (5 ml) of venous blood was aseptically collected from each subject. Serum was separated into Eppendorf tubes after centrifugation then stored at -20°C till needed for analysis. Quantitative determination of IgG and semi-quantitative determination of IgM antibodies against Parvovirus B19 in human serum were measured using ELISA kits (EUROIMMUN AG, Luebeck Germany). Purified antigens are coated to a micro well plate. Antibodies in the patient samples bind to the antigens and are determined during the second incubation step by using enzyme-labeled

anti-human antibodies (the conjugate). The enzyme converts the colorless substrate ($\text{H}_2\text{O}_2/\text{TMB}$) to a blue end product. The enzyme reaction is stopped by adding sulfuric acid and the color of the mixture switches from blue to yellow at the same time. The final measurement is carried out at 450 nm on a photometer using a reference wavelength ≥ 620 nm. Interpretations of the results were done according to the instruction of the manufacturer as follows:

- IgG: Negative (antibody level <0.4 IU/mL), equivocal (antibody level <5.5 IU/mL) positive (antibody level >5.5 IU/mL)
- IgM: Negative (antibody level <0.8 IU/mL), equivocal (<1.1 IU/mL), positive (antibody level >1.1 IU/mL).

Statistical analysis

The data were expressed as the mean $\pm$ standard deviation (SD) or as percentages and ranges as appropriate. Comparisons were made using the Chi-square test using standard equations. The results were reported with $P \leq 0.05$ or $P \leq 0.01$ as the accepted level of significance accordingly.

RESULTS

A total of 349 pregnant women were enrolled in this study and were screened for both IgM and IgG antibodies. Table 1 illustrates the prevalence of both antibodies including the range and mean $\pm$ SD in the study group. Overall, 139 (39.8%) were positive for parvo-virus B19 IgG and 32 (9.2%) had IgM antibody. The remaining 178 (51%) were neither equivocal nor cases with both IgG and IgM.

Tables 2 delineates the prevalence of IgG and incidence of IgM in relation to the demography. The highest prevalence of HPV B19 IgG according to age, trimester, occupation, and number of children was as follows: >35 years (45, 32.4%), second trimester (52, 47.4%), homemakers (89, 64%), ≥ 5 children (45, 32.4%). Statically, the differences of distribution of the Parvovirus IgG in relation to above-mentioned demography were as follows: age >35 years: highly significant ($P \leq 0.01$), second trimester: nonsignificant, homemakers: highly significant ($P \leq 0.01$), ≥ 5 children: highly significant ($P \geq 0.01$). The highest incidence of HPV B19 IgM according to age, trimester, occupation and number of children were as follows: <20 years (13, 40.6%), second trimester (13, 40.6%), homemakers (15, 46.9%), ≥ 5 children (13, 40.6%). Statically, the differences of distribution of the Parvovirus IgM in relation to above-mentioned demography were as follows: age <20 years: significant ($P \leq 0.05$), second trimester:

Table 1: Prevalence of immunoglobulin G and immunoglobulin M antibodies in the study samples

Results	n (%)	Levels range (IU/ml)
IgM+	32 (9.2)	2.1-17.2
IgG+	139 (39.8)	8.3-40.2
IgM- and IgG-	178 (51)	-
Total	349 (100)	

IgM: Immunoglobulin M, IgG: Immunoglobulin G

Table 2: Prevalence of immunoglobulin G and immunoglobulin M antibodies in relation to demographics

Parameters	n	IgG+ (%)	IgM+ (%)
Age group			
<20	36	8 (5.8)	13 (40.6)
≥20-25	79	11 (7.9)	10 (31.3)
>25-30	94	34 (24.5)	9 (28.2)
>30-35	83	41 (29.5)	0 (0)
>35-40	57	45 (32.4)	0 (0)
Total	349	139 (100)	32 (100)
Statistics		$\chi^2=42.547$ df=4, HS ($P\leq 0.01$)	$\chi^2=22.688$ df=4, S ($P\leq 0.05$)
Trimester			
First	137	47 (33.8)	11 (34.4)
Second	109	52 (47.4)	13 (40.6)
Third	103	40 (28.8)	8 (25)
Total	349	139 (100)	32 (100)
Statistics		$\chi^2=1.751$ df=2, NS	$\chi^2=1.197$ df=2, NS
Occupation			
Homemaker	183	89 (64)	15 (46.9)
Day care	86	37 (26.6)	14 (43.8)
Teacher	71	9 (6.5)	3 (9.3)
Clerk	9	4 (2.9)	0 (0)
Total	349	139 (100)	32 (100)
Statistics		$\chi^2=131.129$ df=3, HS ($P\leq 0.01$)	$\chi^2=8.336$ df=3, HS ($P\leq 0.01$)
Number of children			
None	93	16 (11.5)	0 (0)
1-2	121	35 (25.2)	9 (28.1)
3-4	71	43 (30.9)	10 (31.3)
≥5	64	45 (32.4)	13 (40.6)
Total	349	139 (100)	32 (100)
Statistics		$\chi^2=15.101$ df=3, HS ($P\leq 0.01$)	$\chi^2=11.75$ df=3, S ($P\leq 0.05$)

HS: Highly significant, NS: Not significant, S: Significant,

IgM: Immunoglobulin M, IgG: Immunoglobulin G

nonsignificant, homemakers: highly significant ($P \leq 0.01$),
 ≥ 5 children: significant ($P \geq 0.05$).

DISCUSSION

To the best of our knowledge, no published data are available on the prevalence of HPV B19 among pregnant women in Erbil governorate, hence this study can be considered the first study of such quality to deal with and inspect the prevalence and associated risk factors of such an infection among these women. Maternal primary infection with cytomegalovirus (CMV), HPV B19, and rubella virus may give rise to fetus and pregnancy complications.^[7] Because the congenital rubella infection is controlled by the vaccine, CMV and HPV B19 are the most paramount causes of clinically significant intrauterine viral infections.^[8]

In the present study, the prevalence of IgG antibody against HPV B19 was 39.8%. In addition, the incidence of IgM antibody against HPV B19 was 9.2%, which is a sign of acute

infection, and signals that B19 is existent in the population. Thus, more than half (51%) of the women were IgG negative, so they are vulnerable to the HPV B19 infection. HPV B19 infection has been revealed in a number of developed countries throughout the world with adult prevalence rates varying from 30% to 60%.^[4] However, few prevalence screening has been conducted in developing countries.^[2]

HPV B19-specific IgG antibody was detected in 65 out of 86 (75.6%) of pregnant women in west Iran.^[9] In other countries, prevalence of parvovirus B19 antibodies was reported in 59.9% of European and 67.7% of non-European women, without significant differences in demographic parameters.^[10] B19 IgG antibodies detected in 46.6% and IgM antibodies in 2.25% of different age groups of childbearing women in Makkah, KSA.^[11] In another study involving 231 women in Nigeria, 45 (19.5%) were positive for parvovirus B19 IgG, 10 (4.3%) were positive for parvovirus B19 IgM.^[12] IgG prevalence was 61% among the women of childbearing age in Tripoli, Libya, while the incidence of IgM was 5%.^[13]

Divergence in the results of the present study and those aforementioned studies may be due to ELISA techniques and populations variables.^[14] The seroprevalence of HPV B19 seems to be variable worldwide. Diversified factors are renowned to have an impact on the seroprevalence including age, geography, climate, socioeconomic status, occupation, race, parity, and working among children.^[8]

Table 2 explicates the prevalence and incidence of IgG and IgM, respectively, in relation to different demographics. Concerning the women age, the highest prevalence rate of B19 IgG antibodies in the present study was found to be 32.4%. This finding was observed in pregnant women aged between 35 and 40 years. In addition, it is noted that the prevalence of IgG antibodies to parvovirus B19 increases with age in a highly significant manner ($P \leq 0.01$) ranging from 5.8% in women below 20 years of age to as high as 32.4% in women aged between 35 and 40 years age. This finding suggests that the seroprevalence of B19 IgG antibodies is dependent on age, which is in harmony with previous reports.^[11,15] A survey in the USA showed a gradual increase in HPV B19 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 continued exposure to the virus.^[13] Other studies in industrialized countries deduced that infection occurs during adult life increasing the seroprevalence rate from ~60% at age 18 years to >80% in geriatric populations.^[14,16]

Parvovirus B19, seropositivity is a synonym of immunity, the increase in seroprevalence with age denotes that, the proportion of individuals liable to parvovirus B19 decreases with age.^[17] Higher incidence of IgM antibodies was detected in the age group of <20 years (40.6%) with a significant difference ($P \leq 0.05$). This decrease in the incidence of IgM with age is in accordance with a study done in Syria which had investigated 273 pregnant women, concluded that women aged between 22 and 26 years had the highest incidence rate

of IgM antibodies (9.4%) while the lowest rate (0%) was noted in women who are older than 37 years.^[18] Another study which had embroiled 231 pregnant women in Oyo State, Nigeria, pointed that highest incidence of parvovirus B19 IgM antibody (10.8%) was in the 22–27 year age group, and lowest was in the 38 years and older age group.^[12] The decrease in the incidence of IgM with age had been proclaimed by considerable studies which elucidated the certainty that younger women had never had prior infection as compared with older women.^[1,4,11,12,16]

Women in their second trimester of pregnancy were found to manifest the highest rates of IgM and IgG antibodies. However, these differences were not statistically significance ($P \leq 0.05$). The present result is in unison with the outcome of a study accomplished by Emiasegen *et al.*^[15] in which highest rate of antibodies were noticed in the second trimester with no significant association. Okojokwu *et al.*^[19] concluded that a positive linking between prevalence of IgG antibodies and trimester while there was no association between incidence of IgM antibodies and trimester. Emiasegen *et al.*^[15] indicated that the observation of nonsignificant association between high levels of antibodies and trimesters may be a result of chance, differences in the study design or ELISA techniques discrepancies in specificity and sensitivity. Parvovirus B19 infection in pregnant women especially in the second trimester can result in hydrops fetalis and fetal loss, fetal anemia, spontaneous abortion, and stillbirth.^[18] In the present study, 40.6% of the pregnant women had evidence of recent infection in their second trimester, thereby indicating that high number of women who were subjected for the study was at risk and having unfavorable birth outcome. The outcome of the highest incidence (40.6%) and prevalence (47.4%) in the second trimester of the gestational age of pregnancy could possibly be clarified as predisposition to infection may be due to hormonal changes with progress in pregnancy.

The current study clarified that occupation and number of children may have an influence on the prevalence and incidence of IgG and IgM respectively. The prevalence of IgG was higher ($P \leq 0.01$) in homemakers and in women living in families with ≥ 5 children (89,64%; 45,32.4%). The incidence of IgM which denote recent infection was higher ($P \leq 0.01$) in homemakers and in women living in families with ≥ 5 children ($P \leq 0.05$) (15,46.9%; 13,40.6%). Diversified studies had announced the impact of occupation and family size on the prevalence and incidence of IgG and IgM respectively. Abiodun *et al.*^[12] and Emiasegen *et al.*^[15] determined that the rate of IgG and IgM antibodies was significantly highest among full-time homemakers, followed by women working in nursery schools, after-school clubs, or day-care centers. Jegede *et al.*^[20] deduced that high positivity observed among full time homemakers could be due to the fact that women are always in touch with children both at home and outside the home. Another possible elucidation for this observation which was suggested by Röhrer *et al.*^[4] and Ghazi^[11] is that children are more prone to infection with this agent and that full-time

homemakers are with their children all day; therefore, their environment potentiates recurrent contact for dissemination by mean of aerosols. The impact of number of children on the prevalence and incidence of IgG and IgM, respectively, had been recorded by numerous studies. Sharifi *et al.*^[14] recalled that the risk of infection compared with nulliparous women increases about several times in women with three or more children. Habibzadeh *et al.*^[21] had concluded that the hazard of infection in pregnant women with one child are three times more than nulliparous women, but this risk for women with three or more children are 7.5 times more. Elnifro *et al.*^[13] and Okojokwu *et al.*^[19] stated that the proportion of the women who had demonstrated IgM and IgG antibodies in a highly significant manner ($P < 0.05$) increased with the number of children in a household. Khameneh *et al.*^[9] assumed that children are the leading sources of transmission and outbreaks can persist for months in schools and day care centers due to the relatively large number of seronegative children that come in close contact with children within this environment. Ergaz and Ornoy^[5] notified that the infection is commonly passed through respiratory tract secretions from adjacent personal contact. This justifies the present finding that those women with more children were more likely to be infected.

CONCLUSIONS

Nearly 51% of women are susceptible to infection. In addition, IgM antibodies were positive in 9.2% of women, indicating that there is an active transmission of the virus in our population, while 39.8% of women are resistant to infection. A correlation was found between prevalence and incidence of parvovirus infection with the age of the women, number of children in the family, and the occupation of the women.

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Conflicts of interest

There are no conflicts of interest.

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