Nigerian Journal of Paediatrics 2007; 34(3&4): 79-84.

Prevalence of Parvovirus B19 Infection among Children in Lagos Aged One to 15 Years

AO Akinsulie*, EO Temiye**, SA Omilabu***, AS Akanmu+, OO Oladipo++.

Summary

Akinsulie AO, Temiye EO, Omilabu SA, Akanmu AS, and Oladipo OO. Prevalence of Parvovirus B19 Infection among Children in Lagos, Aged One to 15 Years. *Nigerian Journal of Paediatrics* 2007; 34: 79.

Background: Human parvovirus B19 affects rapidly dividing cell lines. Infection with the virus can cause a rapid fall in the haemoglobin level of patients, especially those with haemoglobinopathies such as sickle cell disease.

Methods: A prospective, cross-sectional multi-centre study was carried out on 300 children aged one to 15 years, from four hospitals in Lagos metropolis. The aim of the study was to determine the prevalence of Parvovirus B19 infection by measuring the IgG and IgM serum antibody levels against the organism, using Parvovirus B19 IgG and IgM ELISA kits.

Results: The serum levels of the IgG and IgM antibodies were obtained from 245 (81.7 percent) of the 300 subjects recruited for the study. In 139 of these, results for both IgG and IgM were available while those for IgM or IgG antibodies alone were obtained in 66 and 40, respectively. IgM antibodies were present in 39.5 percent (81 out of 205) of the subjects while IgG was present in 55.9 percent (100 out of 179). The highest current infection rate occurred in children less than three years of age, 54 percent of whom had IgM antibodies, while only 20 percent were positive for IgG antibodies. In 139 subjects who had both IgG and IgM antibodies determined, 50 (36 percent) were negative for these antibodies. Forty-nine (35 percent) subjects who were IgM positive were considered as being currently infected with parvovirus B19.

Conclusion: It is concluded that parvovirus B19 infection is common among Nigerian children.

Key words: Parvovirus B19, IgM antibody, IgG antibody, Lagos metropolis.

Introduction

HUMAN parvovirus B19 was discovered in the sera of asymptomatic patients being screened for hepatitis B infection in England in 1975.[1] The virus is a member of the large Parvoviridae family which includes simian parvovirus, feline panleukopenia virus and canine parvovirus.[2,3] Human parvovirus B19 is a single-stranded DNA virus with a predilection for infecting rapidly dividing cell lines such as bone marrow erythroid progenitor cells.[4] Experiments have confirmed that erythroid progenitor cells in cultures of bone marrow and peripheral blood allow the propagation of the virus.[4,5]

The first report of human parvovirus B19 infection was published in 1980.[6] It described two soldiers who had a brief febrile illness and subsequently had the virus detected in their sera. Since then, infection with the virus has been reported worldwide and it has been associated with diseases such as sickle cell disease and erythema infectiosum.[7] Transmission occurs in all age groups throughout the year. The virus is transmitted through respiratory secretions, transfusion of blood and blood products and vertically from mother to foetus and may lead to hydrops foetalis. Recent infection is best detected

College of Medicine University of Lagos

Department of Paediatrics
*Associate Professor.
**Senior Lecturer
Department of Medical Microbiology and Parasitology
***Professor
Department of Haematology and Blood Transfusion
+Associate Professor.
Department of Clinical Pathology
++Senior Lecturer

Correspondence: Akinsulie AO.
E-mail: adebolaakinsulie@yahoo.com

by the B19 IgM antibody assay while the presence of B19 IgG antibodies correlates with a lower risk of infection.[7]

When an individual is infected, viraemia occurs within the first week accompanied by constitutional symptoms such as fever and malaise. Haematological changes such as moderate reduction in haemoglobin level and reticulocyte count occur at the height of viraemia and this may be accompanied by leucopaenia and thrombocytopaenia.[8] Infection with the virus can actually cause a dramatic fall in haemoglobin level of patients with inherited chronic haemolytic anaemias such as sickle cell disease,[9] pyruvate kinase deficiency,[10] thalassaemia[11] and hereditary spherocytosis.[12] Epidemiological studies from several countries have shown that parvovirus infection is common in children.[13,14] However, there is paucity of information concerning parvovirus infection among children in Nigeria, hence the need for this study whose objective was to determine the prevalence of Parvovirus infection among children in Lagos.

Subjects and Methods

A prospective cross-sectional multi-centre study was carried out on 300 apparently healthy children selected consecutively from the follow up paediatric outpatient clinics of two teaching hospitals and two general hospitals in the Lagos metropolis. The study lasted over a period of six months, November 2003 to April 2004. Ethical clearance was obtained from the Ethics and Research Committees of all the four hospitals involved in the study. In addition, written consents of the parents or guardians of the subjects were also obtained.

A sample of five ml of whole blood was obtained from each subject and placed in a sterile plain bottle. The blood was allowed to clot and the serum was separated by centrifugation at 1500 rpm for five minutes. The sera were stored in nunc vials at -20°C until ready for analysis. IBL Parvovirus B19 IgG and IgM ELISA kits (*IBL Hamburg, Germany*) were used for the antibody screening. Samples were tested for the presence of Parvovirus B19 IgG and IgM according to the manufacturer's instructions. Subjects were stratified by age, and sex against the Parvovrus B19 ELISA positive and negative results. The chi square analysis was used to compare IgM and IgG results in individuals in whom the two antibodies were determined.

Results

A total of 300 patients were recruited for the study. Of these, 35 (11.7 percent) were excluded because of non-availability of both IgG and IGM antibody results. A further 20 (6.6 percent) results were not analysed because of clerical error in sample labeling. The remaining 245 (81.7 percent) subjects who had serological results for IgG and/or IgM antibodies formed the basis of this report.

Subjects were aged from one to 15 years with a mean age of 7.8 ± 4.3 years. There were 128 males and 117 females with a male: female ratio of 1.1:1. The mean age of the male subjects at 7.6 ± 3.9 years, was not significantly different from the 7.97 ± 4.3 years for females (t = -0.8, p = 0.42). The grouped

Table 1

Distribution of Subjects by Age and Sex

Age Group (Yrs)	*Sex*		*Total (%)*
	Males (%)	*Females (%)*	
<3	14 (5.7)	12 (4.9)	26 (10.6)
3-5	29 (11.8)	30 (12.2)	59 (24.1)
6-9	44 (18.0)	36 (14.7)	80 (32.7)
10-15	41 (16.7)	39 (15.9)	80 (26.1)
Total	128 (52.24)	117 (47.76)	245 (100)

$X^2 = 0.53$, p =0.91

age distribution for males and females also showed no significant difference in the age groups (Table I; $X^2 = 0.53$, $p = 0.91$).

Serology results for IgM antibodies were obtained in 205 subjects while 179 results were obtained for IgG antibodies. One hundred and two of the 205 subjects tested for IgM antibodies were males, with positive results in 44, while there were 37 positive results in 103 females. There was no sex difference in positivity for IgM antibodies, $X^2 = 1.12$, $p = 0.29$. Similarly, there was no sex difference in the prevalence of IgG antibodies ($X^2 = 0.63$, $p = 0.42$, Table II). The highest current infection rate of 54 percent, as indicated by the presence of IgM antibodies, occurred in children less than three years old. This stabilized to a rate of between 30.6 percent and 44.1 percent in the other age groups. However, only three (20 percent) subjects who were less than three years of age were positive for IgG antibodies. This rate steadily rose to 71.2 percent in the older age groups as demonstrated in Fig. I. The prevalence of IgM antibodies in the different age groups was not significant ($X^2 = 0.07$, $p = 0.8$). However, the rise in the prevalence of IgG antibody with age was statistically significant ($X^2 = 0.07$, $p = 5.01$, $p = 0.03$).

In 139 (56.7 percent) of the 245 subjects, results of both the IgM and IgG antibodies were available. Fifty subjects (36.0 percent) tested negative for both IgG and IgM antibodies indicating that they had never

Table II

Antibody Reactivity to Parvovirus in the Subjects.

Antibody Reactivity	*IgM*			*IgG*			*Total*
	Male	*Female*	*Sub-Total*	*Male*	*Female*	*Sub-Total*	
Negative	58	66	124	45	34	79	203
Positive	44	37	81	51	491	100	181
Total	102	103	205	96	83	179	384
	$X^2 = 1.12$, $p = 0.29$.			$X^2 = 0.63$, $p = 0.42$			

Table III

Comparison of IgM and IgG Serology Reactions in 139 Subjects

		IgG Serology Reactions		
		Negative	*Positive*	*Total*
IgM Serology Reactions	Negative	50 (36.0)	40 (28.8)	90 (64.75)
	Positive	17 (12.2)	32 (23.0) 90	49 (35.25)
Total		67 (48.2)	72 (51.8)	139 (100)

never been infected with parvovirus B19, forty-nine (35.25 percent) had recent infection, while 40 (28.75 percent) had previous infection (Table III).

conformity with this observation where 36.0 percent of the subjects had never been infected. Also, the number of current infection remained almost

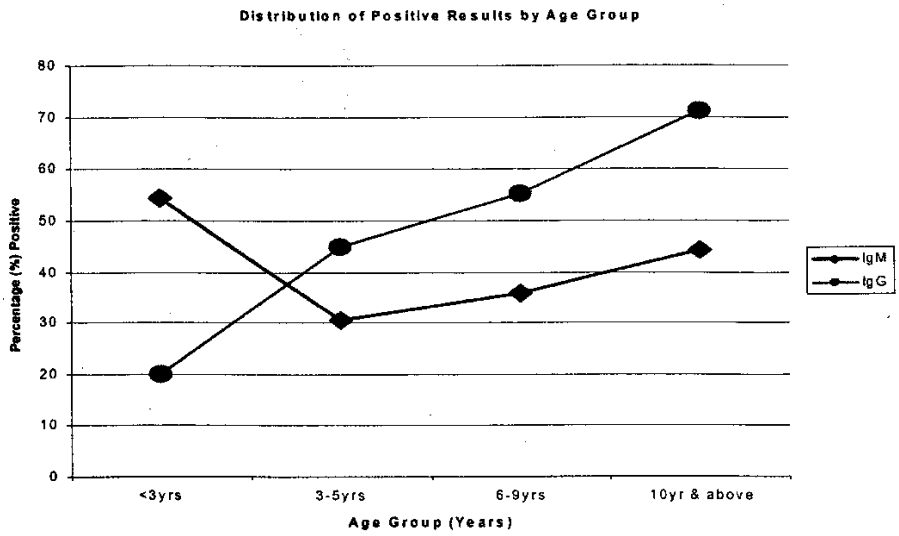

Fig. I: Relationship between age and positive IgM and IgG antibodies to Parvovirus B19

Discussion

This study indicates that Parvovirus B19 infection is common in children in Lagos. Overall, 55.9 percent of the children were positive for IgG antibodies and 39.5 percent for IgM antibodies reflecting a high rate of ongoing infection. This is higher than results obtained from some developed countries. The prevalence rate of IgG in Australian children was 38 percent,[15] 35 percent in Brazilian children aged less than five years,[15] and 27 percent in England and Wales for children aged 10 years or less.[13] However, it is similar to results obtained in Papua New Guinea where the infection rate was up to 60 percent in children aged six years or less.[16] In a neighbouring country of Niger Republic, higher infection rate of 90 percent in children less than two years was reported; this rate fell to 70 percent in children who were 10 years of age or more.[17] However, it is of interest to note that the rate of infection in some Middle Eastern and Asian countries such as Kuwait (17 percent), Saudi Arabia (19 percent) and Singapore (four percent), were much lower than the rate obtained in the present study.[18-20] Some isolated Amazonian tribes and remote islands off the coast of Africa have also been reported to have escaped infection with parvovirus B19.[21]

It has been observed that infection occurs throughout life.[15,21,22] This happens because there are groups of individuals who escaped infection in childhood and adolescence. This study is in constant throughout the age groups after the age of three years as the rise in IgM antibody observed was not significant. The previous observation that the prevalence of positive IgG antibodies rises with age is seen in this study.[15,21,22] The IgG prevalence in children less than three years which was only 20 percent, steadily rose to over 71 percent in those who were 10 years and above. This suggests an endemic mode of transmission of the virus. This is further supported by the high levels of IgM antibody positivity and low levels of IgG antibody in children less than three years who probably formed an initial high unprotected population. The persistence of IgM levels of between 30 and 44 percent in the other age groups is a reflection of sustained high level of transmission of parvovirus throughout childhood and early adolescence in our population. The importance of this in the treatment of febrile children in this area where malaria is also endemic cannot be overemphasized.

Although parvovirus infection is asymptomatic in 20-30 percent of cases,[23] the presence of fever in our region is often assumed to be due to malaria. However, children with fever due to parvovirus infection could be erroneously treated for malaria especially when other causes are not found. This is particularly likely as the typical rash of parvovirus infection comes up approximately 7-10 days after the onset of fever,[23] and the rash which is evanescent,

may not be visible in persons with dark skin such as our study population.[21] The high prevalence of IgM antibody is at variance with the findings in Papua New Guinea and in Tunisian patients with sickle cell anaemia.[16,24] The reason for this is not clear. The high rate of IgM antibodies in this study may reflect the high population density in Lagos which would drive high transmission rate. Furthermore it may reflect a period of outbreak of parvovirus infection in the locality.

It has been estimated that an outbreak occurs every 3-4 years.[15] However, we are not aware of any previous study on the prevalence or the epidemic pattern of parvovirus infection in Nigeria. We therefore assume that the observed rate of IgM antibodies is due to a high and sustained endemicity of parvovirus infection in our population. Further studies on the parvovirus strain involved and the pattern of parvovirus B19 infection in the general population in Nigeria is desirable. The contribution of parvovirus to the incidence of febrile illnesses in Nigeria should also be determined in order to prevent erroneous classification of fever due to this virus as malaria.

Acknowledgement

This paper was supported by a University of Lagos Central Research Grant.

References

1. Cossart YE, Field AM, Cant B, Widdows D. Parvovirus-like particles in human sera. Lancet 1975; 1:72-3.
2. Brown KE, Young NS. The simian parvoviruses. *Rev Med Virol* 1997; 7:211-8.
3. Parrish CR. Pathogenesis of feline panleukopenia virus and canine parvovirus. *Baillieres Clin Haematol* 1995; **8**:57-71.
4. Ozawa K, Kurtzman G, Young N. Replication of the B19 parvovirus in human bone marrow cell cultures. *Science* 1986; **233**:883-6.
5. Serke S, Schwarz TF, Baurmann H, *et al.* Productive infection of in vitro generated haemopoietic progenitor cells from normal human adult peripheral blood with parvovirus B19: studies by morphology, immunocytochemistry, flow-cytometry and DNA-hybridization. *Br J Haematol* 1991; **79**:6-13.
6. Shneerson JM, Mortimer PP, Vandervelde EM. Febrile illness due to aparvovirus. *Br Med J* 1980; **280**:1580.
7. Anderson MJ, Higgins PG, Davis LR, *et al.* Experimental parvoviral infection in humans. *J Infect Dis* 1985; **152**:257-65.
8. Potter CG, Potter AC, Hatton CS, *et al.* Variation of erythroid and myeloid precursors in the marrow and peripheral blood of volunteer subjects infected with human parvovirus (B19). *J Clin Invest* 1987; **79**:1486-92.
9. Serjeant GR, Topley JM, Mason K et al. Outbreak of aplastic crises in sickle cell anaemia associated with parvovirus-like agent. *Lancet* 1981; **2**:595-7.
10. Duncan JR, Potter CB, Cappellini MD, Kurtz JB, Anderson MJ, Weatherall DJ. Aplastic crisis due to parvovirus infection in pyruvate kinase deficiency. *Lancet* 1983; **2**:14-6.
11. Rao KR, Patel AR, Anderson MJ, Hodgson J, Jones SE, Pattison JR. Infection with parvovirus-like virus and aplastic crisis in chronic hemolytic anemia. *Ann Intern Med* 1983; **98**:930-2.
12. Lefrere JJ, Courouce AM, Girot R, Bertrand Y, spherocytosis revealed by human parvovirus infection. *Br J Haematol* 1986; **62**; 653-8.
13. Cohen BJ, Buckley MM. The prevalence of antibody to human parvovirus B19 in England and Wales. *J Med Microbiology* 1988; **25**:151-3.
14. Anderson LJ. Role of parvovirus B19 in human disease. *Pediatr Infect Dis J* 1987; **6**:711-8.
15. 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**: 449-57.
16. Wildig J, Mueller I, Kiniboro B, Maraga S, Siba P, Cossart Y. Seroprevalence of antibodies to parvovirus B19 among children in Papua New Guinea. *Am J Trop Med Hyg* 2007; **77**:354-7.
17. Jones PH, Pickett LC, Anderson MJ, Pasvol G. Human parvovirus infection in children and severe anaemia seen in an area endemic for malaria. *J Trop Med Hyg* 1990: **93**: 67-70.
18. Alsaeid K, Alsaeid M, Essa S, Dimitrov D, Pacsa A. Seroprevalence of human parvovirus B19 in children of a desert region. *Ann Trop Paediatr* 1996; **16**: 255-7.
19. al-Frayh AR, Bahakim H, Kidess E, Ramia S. IgG and IgM antibodies to human parvovirus B19 in the serum of patients with a clinical diagnosis of infection with the virus and in the general population of Saudi Arabia. *J Infect* 1993; **27**: 51-5.
20. Matsunaga Y, Goh KT, Utagawa E, Muroi N. Low prevalence of antibody to human parvovirus B19 in Singapore. *Epidemiol Infect* 1994; **113**: 537-40.

21. Young NS, Brown KE. Mechanisms of disease: Parvovirus B19. *N Engl J Med* 2004; 350: 586-597.
22. Koch WC, Adler SP. Human parvovirus B19 infections in women of childbearing age and within families. *Pediatr Infect Dis J* 1989; 8:83-7.
23. Louisiana office of public health- infectious disease control manual; Erythema infectiosum (EI) Parvovirus infection. Assessed at www.oph.dhh.state.la.us
24. Regaya F, Oussaief L, Bejaoui M, Karoui M, Zili M, Khelif R. Parvovirus B19 infection in Tunisian patients with sickle-cell anemia and acute erythroblastopenia. *BMC Infect Dis* 2007; 7: 123