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**Parvovirus B19 Prevalence among Children of African Descent in Sokoto North Western Nigeria**Ibrahim, K.\*<sup>1</sup>, Muhammad, M.B.<sup>1</sup>, Erhabor, O.<sup>1</sup>, Adias, T.C.<sup>1</sup>, Udomah, F.<sup>1</sup>, Abdulrahman, Y.<sup>1</sup>, Onuigwe, U.<sup>1</sup>, Okwesili, A.<sup>1</sup>, Ibrahim, B.A.<sup>1</sup>, Buhari, H.<sup>1</sup>, Zama, I.<sup>1</sup>, Erhabor, T.<sup>2</sup>, Egenti, B.N.<sup>3</sup>Department of Haematology, School of Medical Laboratory Science, Usmanu Danfodiyo University, Sokoto, Nigeria<sup>1</sup>, Medical Laboratory Science Council of Nigeria<sup>2</sup>, Department of Community Medicine, University of Abuja, Abuja, Nigeria<sup>3</sup>.

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**Abstract**

Human Parvovirus B19 (HPVB19) belongs to the family *Parvoviridae* and it causes *Erythema infectiosum*, aplastic crises in persons with blood disorder and prolonged anaemia in immuno compromised persons. Haematological abnormalities are among the most common manifestation of advanced parvovirus B19 infection. This aim of this study was to determine some haematological parameters and parvovirus B19 IgG antibody among children attending Emergency Paediatric Unit (EPU) of Specialist Hospital Sokoto (SHS). The study population included Ninety-six children attending Emergency Paediatric Unit of SHS (comprising of 57 Males and 39 Females). Prevalence of Parvovirus B19 IgG antibody and the association of some Haematological parameters of Packed Cell Volume (PCV), Platelet Count (PLC) and Total Leukocyte Count (TLC) were determined. Plasma samples from subjects were analysed for HPV B19 IgG antibodies by ELISA while the haematological parameters were analysed using the Mytic 5-part differential haematology analyzer (Orphee, Switzerland). Data obtained was analyzed using statistically. Of the total number of subject tested, 33(34.4%) were positive for Parvovirus B19 antibody and 63(64.6%) had no detectable parvovirus B19 IgG antibody. The mean  $\pm$  standard deviation of some haematological parameters as observed in the study subject (children) were  $32.8 \pm 0.5\%$ ,  $5.18 \pm 0.08$  and  $264.39 \pm 6.67$  for PCV TLC and PLC respectively. Children that were positive for Parvovirus B19 IgG antibody had a mean PCV of 31.80%, TLC of  $4.70 \times 10^9$  and PLC of  $271 \times 10^9$ . The prevalence of parvovirus B19 IgG antibody

was higher among children within age group of 1-5 years (23%) followed by 6-10 years (7%) and 11-15 years (3%) ( $P=0.88$ ). The prevalence of parvovirus B19 IgG antibody was higher among male children (20%) compared to female children (13%) ( $p=0.86$ ). It is recommended that clinicians caring for these patients be made aware of the existence of this virus as well as the possible haematological alterations that could accompany it in our environment. Hospital laboratories should be encouraged to introduce diagnostic tests for parvovirus B19 infection.

**Keywords:** Parvovirus B19; Children; Haematological parameters; Specialist Hospital, Sokoto, Nigeria.

**Introduction**

Parvovirus is the common name applied to all the viruses in the Parvoviridae taxonomic family. Parvoviruses are linear, non-segmented single-stranded DNA viruses, with an average genome size of 5000 nucleotides. Parvoviruses are among the smallest viruses (18–28 nm in diameter) (Fonseca, 2018). Parvovirus B19, the first known parvovirus to infect humans, was discovered in London by Australian virologist Yvonne Cossart (Wildig, 2010). Cossart and her group were focused on hepatitis B and were processing blood samples when they discovered a number of "false positives" later identified as parvovirus B19. The virus is named for the patient code of one of the blood bank samples involved in the discovery (Heegaard *et al.*, 2002).

Parvovirus B19, which causes fifth disease in

children. It is a member of the Erythrovirus genus of the Parvoviridae. Prior to 2014, it was also the name applied to a genus within the subfamily Parvovirinae, but this has been amended to genus *Protoparvovirus* to avoid confusion between taxonomic levels (Nelson *et al.*, 2008). Parvoviruses that infect vertebrate hosts make up the subfamily Parvovirinae, while those that infect arthropods (currently only known to infect insects or shrimp) make up the subfamily Densovirinae. Transmission of the virus may occur at any age. This virus can be transmitted through respiratory secretion, transfusion of blood or blood product, or virtually from mother to foetus and may lead to hydrops foetalis (Anderson *et al.*, 1985).

Human parvo virus B19 has been associated with several diseases. Aplastic crisis in patient with chronic haemolytic anaemia, erythema, hydrops foetalis and arthritis are among the common diseases caused by this virus infection. In the period between July 1991 and March 1992, 48 patients with aplastic crisis were hospitalized at Saudi Aramco-Dhahran Health center. Forty-six patient had homozygous sickle cell disease, one had haemoglobin H disease and one had hereditary elliptocytosis. Evidence of recent human parvovirus infection was present in 91% of cases. Leukopenia was presence in 21%, neutropenia in 27% and thrombocytopenia in 41% (Mallouh and Qudah, 1995). This differs from previous reports in which red blood cell aplasia causing anaemia was the commonest haematologic finding reported in most patient (Yetgin *et al.*, 2004).

Parvovirus B19 (properly called human parvovirus B19) infects only humans with different symptoms, depending on individual age and overall health. Fifth disease is the most common illness caused by parvovirus B19. It can also cause the body to temporarily stop making new red blood cells. The disease is more severe in children; this can lead to transient aplastic crisis, hydrops foetalis, congenital anaemia, pure red cell aplasia, or persistent anemia (Anderson *et al.*, 1985). Persistent anaemia (in immuno-deficient and immuno-compromised patients and in the fetus), hydrops fetalis and congenital anaemia (Koch 1990) are common manifestation

associated with parvovirus B19 infection.

The study of Haematological abnormalities in children with parvovirus B19 is very important in order to prevent haematological complication that may arise during the infection. Furthermore, no study has been conducted on parvovirus B19 and its effect on haematological parameters in Sokoto. The study would provide haematological information that could be used in taking preventive actions in management of children with parvovirus B19 infection. The aim of this study was to determine the prevalence of parvovirus B19 antibody and some haematological parameters among children attending the Emergency pediatric unit of Specialist Hospital Sokoto (SHS).

### Methodology

The study was carried out using Parvovirus B19 ELISA kit (**Demeditec Diagnostics GmbH, Germany**). The test is a quantitative method for determination of the presence of Parvovirus B19 IgG antibody in serum of children below 15 years attending to the paediatric unit of SHS. Full blood count was determined using the 5-part differential haematology analyzer (Orphee, Switzerland).

### Study Design

The present case study investigated the prevalence of Parvovirus B19 and the FBC parameters and among 96 consecutively-recruited children attending the Pediatric unit of SHS Sokoto, Nigeria.

### Study Site

The study was conducted at the Department of Haematology in the Faculty of Medical Laboratory Science, in Usmanu Danfodiyo University Sokoto in collaboration with Paediatric unit of SHS, Sokoto. The study sites and participating hospital have enabling environment to carry out this study. Sokoto State is located extreme North West of Nigeria near to confluence of Sokoto River and the Rima River. With an average annual temperature of 28.3°C (82.9°F), Sokoto is on the whole a very hot area. However, maximum day time temperature is most of these generally under 47°C (104°F). The warm months are February to April when

daytime temperature is on the excess of 40°C (113°F). The rainy season is from June to October during which showers are daily occurrence. Report from the 2007 national population commission indicated that the State had a population of 3.6 Million (Udo *et al.*, 1993). The Paediatric Unit is a Department in SHS, Sokoto, providing a continually improving healthcare services to children below the age of 15year. Majority of patient received at this hospital are people of Sokoto, Kebbi and Zamfara states as well as Children from the neighboring Niger Republic.

### Sample Size Calculation

The sample size was determined according to Cochran (1999) for population that is >10,000 using the formula:  $n = (z)^2 pq \div d^2$

Where:

n = minimum sample size

z = standard normal deviation (1.96)

p = proportion of success or prevalence (50%)

q = 1 - p

d = tolerance limit, the minimum is 0.05.

$n = (z)^2 pq \div d^2$

$n = (1.96)^2 \times 50\% \times 1-p \div 0.05^2$

$n = 3.8416 \times 0.5 \times 1-0.5 \div 0.0025$

n=384

### Study Subjects

A total of 100 subject aged 1-15 years were used for the study comprising of 57 male and 43 females attending EPU of SHS, Sokoto North Western Nigeria.

### Inclusion Criteria

All children within the age range of 1-15years whose parents/guardians have offered verbal informed consent for their ward to be recruited as subjects were consecutively recruited in to this study from among children visiting the EPU of SHS in Sokoto, Nigeria.

### Exclusion Criteria

All children >15years and those whose parents/guardians did not give verbal informed consent for their ward to be recruited as subjects were excluded from the study.

Ninety-six children who met the eligibility criteria for the study were consecutively

recruited as subject for this cross-sectional study to avoid bias. Socio-demographic data collected was obtained using a self-administered questionnaire from each participant. Data collected include age, gender, tribe, religious and level of education.

### Statistical Analysis

The data collected was recorded on an excel spreadsheet and later subjected to statistical analysis using statistical software (SPSS Version 20.0). Results were expressed as mean and standard deviation. Differences in values based on socio-demographic variables of subjects was determined and compared statistically. A p-value of  $\leq 0.05$  was considered as significant in all statistical comparisons.

### Ethical Consideration

Ethical clearance for the study was sought and obtained from the ethics and research committee of SHS Sokoto before the commencement of the study.

### Informed Consent

Verbal informed consent was obtained from parents/guardians of all study participants and socio-demographic information was collected using a questionnaire.

### Questionnaire

A questionnaire was distributed to all consenting parents to collect socio-demographic data of study subject.

### Sample Collection

Blood samples (3milliliters) were aseptically collected from subjects attending the paediatric unit of SHS Sokoto. The Serum level of parvovirus B19 IgG antibody was determined using Parvovirus B19 IgG antibody ELISA kit and the Full blood count was determined using the 5-part differential haematology analyzer.

### Principle of the Test Method (Parvovirus B19 IgG antibody)

The Demeditec Parvovirus B19 IgG enzyme immunoassay kits (Demeditec Diagnostics, Germany) were used for the in vitro qualitative and semi-quantitative measurement of the amount of immunoglobulin class antibodies for



B19 present in the serum. Testing was carried out strictly following the manufacturer's standard operating procedure. The microtiter wells were coated with recombinant parvovirus B19 antigen (VP1 proteins). The antigen was derived from the entire VP1 unique region of B19. The test kits are designed for the measurement of parvovirus infections in humans only. Prevalence was defined by the presence of B19 IgG antibodies in the tested sera. Positive or negative cases were determined by comparing the absorbance value of each sample with that of the cut-off value. Based on the manufacturer's instructions, specimens with an absorbance value less than the cut-off value were recorded as negative while specimens with a value above the cut-off value were recorded as positive.

### Full Blood Count

Full blood count testing was carried out using 5-part differential Mythic 22 CT, 2008 Haematological analyzer (Orphee, Sweden). The principle of the analyzer is based impedance counting was developed by Wallace Coulter in 1956. The Coulter counter system is based on the principle that RBC or WBC is a poor conductor of electricity compared to the diluents such as saline. When the diluent is displaced by cells, it causes a measurable change in resistance. The cells are allowed to pass through an aperture through which an electric current is flowing. Cell passing through the aperture displace the diluents; and being bad conductors of electricity, increase the resistance which is counted as a voltage pulse, which are converted to digital recording. The cell suspension is drawn through the aperture with the help of a vacuum pump into a system of tubing.

### Result:

A total of nine six (96) children attending EPU of Specialist Hospital Sokoto comprising of 57

male and 39 females with mean age of  $7.5 \pm 6.5$  years constituted the subject for this study. Of the total number of subject tested, 33(34.4%) were positive for Parvovirus B19 antibody and 63(64.6%) had no detectable parvovirus B19 IgG antibody. Table 1 show the prevalence of parvovirus B19 IgG among children attending Emergency Paediatric Unit of SHS. The mean  $\pm$  standard deviation of some haematological parameters as observed in the study subject (children) were  $32.8 \pm 0.5\%$ ,  $5.18 \pm 0.08$  and  $264.39 \pm 6.67$  for PCV TLC and PLC respectively. Table 2 shows the mean values for some haematological parameters among children attending EPU of SHS. Children that were positive for Parvovirus B19 IgG antibody had a mean PCV, TLC and PLC of 31.80%,  $4.70 \times 10^9$  and  $271 \times 10^9$  respectively. Table 3 shows the Haematological changes as observed in the PCV, TLC and PLC in subject with Parvovirus B19 IgG antibody. The prevalence of parvovirus B19 IgG antibody was higher among children within age group of 1-5 years (23%) followed by 6-10 years (7%) and 11-15 years (3%) ( $p=0.88$ ). The prevalence of parvovirus B19 IgG antibody was higher among Male children (20%) compared to Females children (13%) ( $p=0.86$ ). Table 4 comparison of age and some haematological parameters of children studied. Result obtained from Table 5 shows the effect of gender on haematological parameters of children. Table 6 shows the prevalence of parvovirus B19 among children of different age group. Result obtained shows that the prevalence was highest among children within age group of 1-5 (23%) followed by 6-10 (7%) and 11-15(3%) respectively ( $p=0.88$ ). Table 7 show the prevalence of parvovirus B19 among children of different gender. Result obtained in this table shows a high prevalence among Male children (20%) compared to Females children (13%) ( $p=0.86$ ).

**Table 1: Prevalence of parvovirus B19 IgG Among children attending Emergency Paediatric Unit of SHS**

Parvovirus B19	No of children tested	Percent (%)
Reactive	33	34.4
Non-reactive	63	65.6
Total	96	100



**Table 2: Some Haematological parameters among children attending EPU of SHS**

Haematological parameters	Mean Value	Standard Deviation
PCV (%)	32.80	8.72
PLT ( $\times 10^9/L$ )	5.18	1.91
TLC ( $\times 10^9/L$ )	264.39	72.91

**Table 3: Some Haematological parameters among children with parvovirus B19 IgG**

Parvovirus B19 IgG Result	Haematological parameters (Mean value)		
	PCV (%)	PLT ( $\times 10^9/L$ )	TLC ( $\times 10^9/L$ )
Reactive	31.79	271	4.70
Non-Reactive	33.09	261	5.35

**Table 4: Comparison of age and Haematological parameters of children attending EPU of SHS**

Age Group (years)	Haematological parameters (Mean value)		
	PCV (%)	PLT ( $\times 10^9/L$ )	TLC ( $\times 10^9/L$ )
1-5	32.80	260	5.07
6-10	32.40	288	5.24
11-15	33.40	264	5.15

**Table 5: Comparison of gender and Haematological parameters of children attending EPU of SHS**

Gender	Haematological parameters		
	PCV (%)	PLT ( $\times 10^9/L$ )	TLC ( $\times 10^9/L$ )
Male	32.5	263	5.42
Female	33.15	263	4.80

**Table 6: Comparison of Age and prevalence of parvovirus B19 IgG among children attending EPU of SHS.**

Age group (years)	Parvovirus B19 IgG Result		Total
	Reactive N (%)	Non – Reactive N (%)	
	1-5	23 (69.7)	
6-10	7 (21.2)	11 (17.5)	18
11-15	3 (9.1)	7 (11.1)	10
Total	33 (100)	63 (100)	96

**Table 7: Comparison of Gender and prevalence of parvovirus B19 infection**

Gender	Parvovirus B19 IgG Result		Total
	Reactive	Non -Reactive	
Male	20	37	57
Female	13	26	39
Total	33	63	96

### Discussion

This study indicates that parvovirus B19 infection is common among children in Sokoto. Out of the 96 subjects studied, 34.4% were positive for IgG antibody. Our observed prevalence is higher than a prevalence of 27% obtained in England and Wales for children aged 1-10 years (Cohen *et al.*, 1988). The observed prevalence in this study varies compared to a prevalence of 46.6%, 19% and 4% prevalence observed respectively in Saudi Arabia (Ghazi, 2007), Kuwait, (Al-frayh *et al.*, 1996) and in Singapore (Matsanaga *et al.*, 1994) respectively.

However, the prevalence observed from this study is consistent with the 35% prevalence reported among Brazilian children aged 1-5 years (Kelly *et al.*, 2000). The prevalence of parvovirus B19 IgG antibody in this study is lower compared to a rate obtained in a previous study in Lagos Nigeria which observed a prevalence of 55.9% (Akinsulie *et al.*, 2010). Similarly, a previous report in neighboring Niger Republic observed a 70% parvovirus B19 prevalence (Jones *et al.*, 1990). *B19 is global and common infectious pathogen in humans. The prevalence of IgG Antibodies directed against B19 ranges between 2 to 15% in children 1 to 5 years old, 15 to 60% in children 6 to 19 years old, 30 to 60% in adult and more than 85% in the geriatric population (Cohen et al., 1988). Women of child bearing age show an annual seroconversion rate of 1.5% (Koduri, 1988). Although antibody is prevalent in the general population, viraemia or presence of viral DNA is rare. The frequency of B19 viraemia in voluntary blood donors has been estimated at rate of 1:167 to 1:35000 (Shade et al., 1986). As opposed to the many studies on B19 DNA in the bone marrow of healthy individuals is limited. While no serum was available for comparison, one*

*study discovered B19 DNA in bone marrow of 45 (9%) healthy bone marrow donors (Cassinotti et al.,1996), and another reported no evidence of B19 DNA in the bone marrow of 13 bone donors (Foto et al.,1993). The peak incidence of erythema infectiosum is in late winter and early spring. Small epidemics at intervals of a few years are typical. The virus is spread by respiratory droplets (Anderson et al., 1987), by blood products especially pooled factor XIII and IX concentrates (Jordan et al., 1998) and transplacentally during pregnancy.*

Haematological changes are common in Parvovirus B19 infection. In this study mean  $\pm$ standard PCV, TLC and PLC count of children positive for Parvovirus B19 were  $32.8 \pm 0.5\%$ ,  $5.18 \pm 0.08$  and  $264.39 \pm 6.67$  respectively. Although parvovirus B19 infection is asymptomatic in 20-30 cases, the presence of fever and decrease in haematological count in our region is often assumed to be due to malaria and sickle cell anaemia. However, children with fever due to parvovirus B19 infection could be erroneously treated for malaria especially when other causes are not found. This is particularly likely as the typical rash of parvovirus B19. Infection comes up approximately 7-10 days after the onset of fever and the rash which is evanescent may not be visible in persons with dark skin such as our study population (Young *et al.*, 2004). The high prevalence observed in this study may reflect a period of outbreak of parvovirus infection in the locality even though no such study has ever been carried out in this part of the country. Human parvo virus B19 has been associated with several diseases. Aplastic crisis in patient with chronic haemolytic anaemia, erythema, hydrops foetalis and arthritis are among the common diseases caused by this virus infection. In the period between July 1991

and March 1992, 48 patients with aplastic crisis were hospitalized at Saudi Aramco-Dhahran Health center. Forty-six patient had homozygous sickle cell disease, one had haemoglobin H disease and one had hereditary elliptocytosis. Evidence of recent human parvovirus infection was present in 91% of cases. Previous report (Wildig et al., 2010) that investigated Parvovirus B19 infection and severe anaemia in Kenyan children indicated that High B19 IgM levels were significantly associated with severe anaemia.

Leukopenia was presence in 21%, neutropenia in 27% and thrombocytopenia in 41%. This differs from previous reports in which red blood cell aplasia causing anaemia was the only haematologic finding reported in most patient (Girei *et al.*, 2010).

Parvovirus B19 infection was higher among children in the 1-5 years age group (69.7%) compared to 21.2% and 9.1% respectively among children 6-10 years and 11-15 years respectively. It's important to note that some Amazonian tribes and remote Islands off the coast of Africa have been reported to have escape infection with parvovirus B19. It has been observed that infection occurs throughout life (Blumel *et al.*, 2010). This happen because there are group of individuals who escape infection in childhood and adolescence.

The prevalence of parvovirus B19 IgG antibody was higher among male children (20%) compared to females children (13%). The reason for this male gender increased predisposition to parvovirus B19 is unknown. Hormonal factors may potentially play a role.

### Conclusion

In conclusion, the finding in this study indicates a human Parvovirus B19 IgG antibodies prevalence of 34.4% among children with an insignificant decrease in their haematological count in Sokoto State, North Western Nigeria. The presence IgG antibody is an indication of a previous infection and immunity against Human parvovirus B19 infection. A significant number of children 65.6% are not immuned and are thus potentially prone to infection that may

erroneously be considered as malaria such as erythema infectiosum and aplastic crisis.

### Recommendation

From the study result, we recommend that further study to screen large number of children for parvovirus B19 IgG and IgM antibody. We also recommend that haematological parameters should be determined in patient with the infection to avoid misdiagnosis of patient for malaria. There is need for more awareness among clinicians on the clinical signs, diagnosis and management of parvovirus B19 infection and the effect it can potentially have on the haematological parameters of affected children. There is also the need for public awareness on preventive measures to be taken to avoid the infection.

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