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# Seroprevalence of acute human parvovirus B19 viraemia among anaemic children in ibadan city, Nigeria

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ABSTRACT

**Objective**: To determine the seroprevalence of B19V IgM as a measure of acute infection and associated risk factors among < 5 years children at Oyo state, Nigeria. **Methods**: One hundred and sixteen (116) and thirty eight (38) blood samples were individually collected from severe anaemia and age-matched non-anaemic children between 1-60 months old at Oyo state, Nigeria. EDTA anticoagulated blood was tested for their packed cell volume, while sera were tested for human parvovirus IgM antibodies using microhaematocrit centrifuge and Enzyme Linked Immunosorbent Assay, respectively. Interviewer-based questionnaires were used to collect participants' sociodemographic variables. **Results**: Anti-B19V IgM was detected in 17 (14.7%) severe anaemia subjects, whereas, only 2 (5.3%) non-anaemia subjects had B19V IgM. The prevalence of parvovirus B19 IgM antibodywas higher in anaemic subjects than non-anaemic control group. There is significant association between the seroprevalence of anti-B19V IgM and family size ($P$=0.001), number of siblings ($P$=0.032) and education status ($P$=0.01) of anaemic children but seroprevalence of anti-B19V IgM is not significantly associated with gender, family type and age ($P$>0.05). **Conclusions**: The seroprevalence of 14.7% among anaemic children confirm that these infections are endemic in Nigeria. This level of infectivity suggests that there is a high risk of transmission to healthy children as well as children with underlying haemolytic or acquired anaemia in Nigeria.

## 1. Introduction

Severe anaemia (haemoglobin<5.0 g/L) is a main etiology of childhood mortality in malaria endemic areas, especially sub-Saharan Africa[1]. In these areas, most children have mild to moderate anaemia arising from factors which reduce red blood cell survival time and/or inhibit erythropoiesis. These include malaria, HIV, iron deficiency, haemoglobinopathies, protein-energy malnutrition, and other under-reported infections such as human parvovirus B19(B19V)[2].

B19V is the only parvoviridae member associated with human infectious disease[3]. B19V is a small single stranded DNA virus with linear genomes measuring about 5 kb[3]. B19V has been

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associated with various clinical manifestations whose features depend on the interplay between the viral properties, the immune and physiological status of infected persons[4].

B19V infection has worldwide distribution. It is common in children and continues at a low rate at adulthood, and most elderly become sero-positive[5]. Human Immunoglobulin G antibodies to B19V are detectetable in serum 7-14 d after contracting the virus and last for life, providing immunity against most re-infections[5].

B19V is transmitted through the respiratory route, parenterally administered blood and blood products and vertical transmission[5]. Higher rates of B19V infections have been reported among children in some tropical areas[6]. B19V has singular tropism for red cells precursors in the bone marrow, with acute infection causing defective erythropoiesis for 1-2 weeks and complete remission for 3-7 d[7]. The effect of B19V pathogensesis on red cells varies by individual. In apparently healthy adults, haemoglobin level tends to decrease by ~20 g/L[7], whereas higher decline in haemoglobin level have been reported in individuals suffering from severe malaria and iron deficiency[8]. In persons with haemoglobinopathy, a precipitous decline in haemoglobin concentration can be induced through the combination of a high rate of haemolysis and complete cessation of erythropoisis caused by B19V infectrion. This condition is refered to transient aplastic crisis[8].

When an individual comes in contact with B19V, viral replication leads to profuseviraemia that begins to decline when Immunoglobulin M(IgM) is produced on at about 9$^{th}$ day[9]. B19V-induced bone marrow suppression gets abated on the 16$^{th}$ day, and the lowest haemoglobin concentration occurs thereafter[10]. With these, simultaneous detection of anti-B19V IgM and viral DNA is highly indicative of acute B19V infection. B19V IgM usually becomes undetectable after 30-60 d, depending on the initialdegree of immune response and viral load[11].

Both viraemia and halflife of B19V are less predictable and unknow. Even though the virus may become undetectable immediately after infection, clinical studies using highly sensitive nucleic acid amplification tests have shown that B19V DNA can often be detected 180 d after the onset of illness in patients with IgM negative results[12].

In Kenya and Malawi, 2 serological surveys revealed only little evidence of acute B19V infection in all categories of children, whether anaemic or non-anaemic over the course of 12 months of testing[13,14]. There is paucity of published studies on the incidence and prevalence of B19V-associated paediatric anaemia in Nigeria despite the importance of such information in child health policy formulation. In view of this, the current study aim to ascertain the seroprevalence of B19V IgM as a measure of acute infection and associated risk factors among children under five at Ibadan city, Oyo state, Nigeria.

## 2. Materials and methods

### 2.1. Study area

The study was carried out in Ibadan, State capital of Oyo state, Nigeria. Data and samples were collected at Adeoyo Maternity General Hospital, Oni and Sons memorial Hospital, Oluyoro Catholic Hospital, Ibadan central Hospital, all located in Ibadan.

### 2.2. Study population

Study included patients presenting with severe anaemia in the age group 0-5 years (0-60 months) admitted at the Paediatric Unit of Adeoyo Maternity General Hospital, Oni and Sons Memorial Hospital, Oluyoro Catholic Hospital, Ibadan central Hospital, Ibadan, between 28$^{th}$ April and 20$^{th}$ December, 2016. Severe anemia was defined by packed cell volume $\leqslant$20% and non-anaemic as those with PCV of 34%-42% (WHO reference range for age 2-6 years).

### 2.3. Study design

It is a cross-sectional study aimed at determining the prevalence of parvovirus B19 virus in children (0-5 years) in Ibadan.

### 2.4. Samples size and population

Since there is no data on B19V-associated paediatric anaemia in Nigeria, a study was conducted in Papua New Guinea, a neighboring West African country, reported 14.8% IgM antibodies in children between 6 months and 5 years by Wildig *et al*[15]. On this basis, the sample size for the present study was calculated and the minimum sample size was calculated as 100 according to study of Wildig *et al*[15].

A total of 116 blood samples individually collected from consented participants (children at 5 years) with severe anaemia admitted to Adeoyo Maternity General Hospital, Oni and Sons memorial Hospital, Oluyoro Catholic Hospital, Ibadan central Hospital. Control population of non-anaemic children with same age range presenting with febrile illness (38) was taken as control.

### 2.5. Informed consent and ethical approval

The study was explained to parents/guardians of enrolled participants, and they gave their oral and /or written informed consent. Participants were all confirmed seronegative for HIV, malaria microscopy negative and no history of malnutrition. An interviewer-based questionnaire was used to obtain bio-data and risk factors variables from parents of these participants in accordance with the Declaration of Helsinki. Parents/guardians filled questionnaires on behalf of their children (Ethnical committee approval No. AD13/479/782).

### 2.6. Sampling techniques

Venous (2.0 mL) blood was collected in EDTA anticoagulated bottle from each participant through venipuncture. The EDTA anticoagulated blood samples were used for measure of packed cell volume. Remaining whole blood was centrifuged at 3 000 rpm for 10 min and the resulting plasma sample were separated into cryovials for serological analysis. The plasma samples were stored at -20 ℃and analyzed within 48 h.

### 2.7. Laboratory assay

Plasma from all participants were tested for the presence of parvovirus B19 IgM antibodies using parvovirus B19 IgM ELISA kit by IBL international, USA. The test was performed according to the manufacturer's instructions.

### 2.8. Principle of the test

The principle is based on the sandwich ELISA (Enzyme-linked Iimmunosorbent Assay) technique. The absorbance of the final reaction product was measured at 450 nm using an ELISA micro-well plate reader.

### 2.9. Statistical analysis

Data obtained were analyzed using SPSS software version 24 (IBM Corporation, Armonk, NY, USA). Ages were presented as percentages and mean ± standard deviation. Categorical data were presented in tables and bar charts. *Chi*-square was used to determine the association between seroprevalence of anti-B19V and the risk factors/sociodemographic variable studied. Statistical signifcance was infeered from $P<0.05$ at a confidence interval of 95%.

## 3. Results

One hundred and sixteen (116) children presenting with severe anaemia including 48 females and 68 males [mean age: (12.2±3.8) months; female to male ratio of 1:1.4] and 38 age-matched non-anaemic children including 19 females and 19 males (mean age: (12.3 ± 4.5) months; female to male ratio 1:1] were enrolled in this study.

Parvovirus B19 IgM was detected in 17(14.7%) subjects with severe anaemia, whereas, only 2(5.3%) non-anaemic subjects had B19V IgM seropositivity. The prevalence of Parvovirus B19 IgM antibody was higher in anaemic patients than non-anaemic control group.

The prevalence of anti-B19V IgM was higher in female subjects (10, 20.8%) than in male subjects (7, 10.3%) for anaemia children ($P$=0.138). The prevalence of B19V IgM was highest in anaemic children living in homes of more than 8 people living together (3, 100.0%) and least in children in homes with 3-5 people living together (9, 11.5%).

Parvovirus B19 IgM was significantly higher in children with mother having between >4 offsprings (4, 36.4%) than children with mother having between 1-4 offsprings (13, 12.4%) ($P$=0.032). The prevalence of parvovirus B19 IgM was higher among anaemic children from polygamous families (3, 37.5%) compared to those from monogamous families (14, 12.9%). The prevalence of B19V IgM is relatively higher among anaemic children attending school (16, 20.5%) than those who are not yet in school (1, 1.7%) (Table 1). There is significant association between the prevalence of B19V IgM and family size ($P$=0.001), number of siblings ($P$=0.032) and education status ($P$=0.01) of anaemic children but not significantly associated with their gender, family type and age ($P$>0.05) (Table 1).

**Table 1**
Risk factors of B19V IgM antibodies in anaemia children.

| Risk factors | | Total | Number of anaemia(%) | *P* |
|---|---|---|---|---|
| Gender | Male | 68 | 7(10.3) | |
| | Female | 48 | 10(20.8) | |
| | Total | 116 | 17(14.7) | 0.138 00 |
| Family size (number) | 3-5 | 78 | 9(11.5) | |
| | 6-8 | 35 | 5(14.3) | |
| | >8 | 3 | 3(100.0) | |
| | Total | 116 | 17(14.7) | 0.000 01* |
| Parity (number of siblings) | 1-4 | 105 | 13(12.4) | |
| | >4 | 11 | 4(36.4) | |
| | Total | 116 | 17(14.7) | 0.032 00* |
| Family type | Monogamous | 108 | 14(12.9) | |
| | Polygamous | 8 | 3(37.5) | |
| | Total | 116 | 17(14.7) | 0.058 00 |
| Education | Schooling | 78 | 16(20.5) | |
| | Not schooling | 58 | 1(1.7) | |
| | Total | 116 | 17(14.7) | 0.001 00* |

Note: *Significant association determined by *Chi*-square test.

Children within the age group of 41-51 months had the highest prevalence of B19V IgM anitibodies and least in those within 1-10 months. There is no signiffcant difference between the seroprevalence of B19V IgM and age of children ($P$=0.647) (Figure 1).

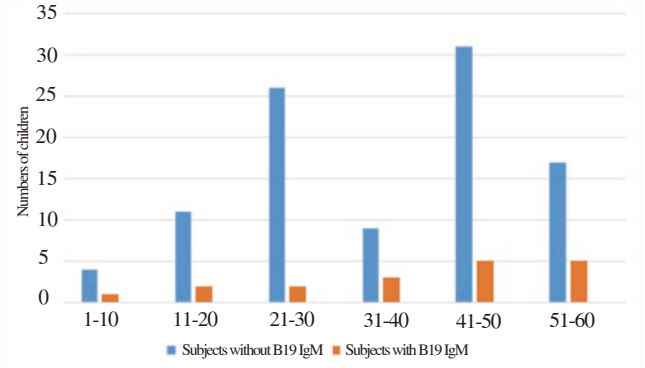


**Figure 1.** Age distribution(Month) of B19V IgM among severe anaemic children. Df=5; *Chi*-square=3.343; $P$=0.647.

## 4. Discussion

In this study, anti-B19V IgM was significantly higher in anaemic children compared to the non-anaemia subjects. Presence of IgM antibodies indicates acute infection; parvovirus IgM antibodies presence in 14.7% of the patients is suggestive of significant association of severe anaemia with parvovirus infection, this is in support of studies by Wildig *et al*[15] and Jones *et al*[16].

The prevalence of B19V in this study is similar to study of children presenting with severe anaemia carried out in Papua New Guinea where a prevalence of 14.8% in anaemia cases and 8.9% among control groups were reported, also in Lagos, Nigeria with a prevalence of 14.3 % in sickle cell patient. The finding of association between acute B19V infections is in consosnance with the reports from Niger Republic[16]. However, this did not corroborate with findings from two other reports from Kenya and Malawi[13, 14]. The difference in the findings from the latter studies may be due to coincidence of study time with period of low B19V transmission in the respective communities.

This study reveals that children between 41-51 months of age have the highest prevalence of B19V infection and 1-10 months children had the least prevalence. This could be because children in the 41-50 months age group are the mostly socially active and hence this may explain the high prevalence of B19V among them.

Parvovirus B19 infection is transmitted through respiratory route. Hence overcrowding and congestion are risk factors of B19V acquisation. This may explain the high prevalence of the infection among large family size such as those residing in homes with >8 peoples (100%), large parity siblings and polygamous family.

Learning activities and environment create an avenue for children to socialize and increase the exposure of children to infection compare to children socialization due to indoor keeping. Hence, children who are yet to start school have minimal risk of contact with peers, this may be considered while explaining reason for high prevalence in anaemic children in school compare children not yet in school. Hence, this study identified family size, high parity, and nature of school attended by children as risk factors incriminated in the spread of parvovirus B19 with family size as the lead, this finding is in support with a study carried out in Lagos[17].

The seroprevalence of 14.7% among anaemic children confirms that these infections are endemic in Nigeria. This level of infectivity suggests that there is a high risk of transmission to healthy children as well children with underlying haemolytic or acquired anaemia in Nigeria.

## Conflict of interest statement

The authors report no conflict of interest.

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