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# HUMAN PARVO VIRUS B19 IN NIGERIA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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## ABSTRACT

Human Parvovirus B19 is an important pathogen that causes Erythema infectiosum (also known as fifth disease) in children, non-immune hydrops fetalis in pregnant women, aplastic crisis in sickle cell patients, anaemia in immunocompromised patients as well as arthralgia in seronegative immunocompetent individuals worldwide. Many studies on human infection with parvovirus B19 have been reported globally. However, a systematic review and meta-analysis of the infection has not been published in Nigeria. This study extracted articles pertaining to B19V infection in humans in Nigeria using four databases: Google Scholars, PubMed, web science, and African Journals OnLine (AJOL). We retrieved 24 articles related to B19V infection in Nigeria and these articles were retrieved from 1 January 2009 to 20 May 2024. It was estimated that the overall prevalence of humans with parvovirus B19 in the selected period was 25.9% (1377/4275). In the subgroup analysis, the prevalence of B19V was estimated to be 66.9%, 46.7%, 40.6%, 26.7% and 13.5% in the North West, North East, North Central, South South and South West of Nigeria, respectively. In sickle cell patients, the prevalence of B19 V was 34.2%. (17.7-57.0). By contrast, the prevalence of B19V in HIV patients was only 3.3%. (0.7-14.8). The prevalence of parvovirus B19 infection in pregnant women, sickle cell patients, children, blood donors, HIV patients, and hepatitis patients in Nigeria was found to be significantly different in the current review. It is recommended that periodic infection screening be incorporated into the routine clinical care of these patients.

**Keywords**: Human, Meta-analysis, Nigeria, Prevalence, Parvovirus B19

## INTRODUCTION

Human Parvovirus B19 virus (B19V) is a small single-stranded DNA virus in the genus Erythroparvovirus (family: Parvoviridae) with high target for red blood cells (RBCs) progenitors, that may lead to temporary suppression of erythropoiesis [1, 2]. Parvovirus B19 is mainly transmitted person-to-person through the respiratory secretions. Infections is also transmitted in seronegative adults through other routes such as hematogenous (Blood transfusion, organ transplants etc) as well as through vertical transmission during pregnancy [3-5].

B19V infection is common during childhood but also occurs primarily in at-risk individuals, such as pregnant women and a broad range of immunocompromised individuals (AIDS and organ transplant patients) [6, 7]. Infection in immunocompetent adults is characterised by transient anaemia, but may cause hydrops foetalis, spontaneous abortion, or intrauterine foetal death (IUFD) during pregnancy, and severe aplastic crisis in other at-risk groups. Global prevalence studies show that in urban areas the antibody prevalence increases up to 50-80% in those aged 15-20 years. Prevalence of seronegative adult individuals range from 40-60% [8, 9]. Diagnosis is primarily based on the detection of specific antibodies by enzyme-linked immunosorbent assay or detection of viral DNA by conventional PCR or qPCR [10]. Treatment of persistent infection with immunoglobulin reduces the viral load and results in a marked resolution of anaemia. Red blood cell transfusion is adequate to treat immunocompetent patients with transient aplastic crisis. Considering the significance of parvovirus among the human population, an overview and analysis of infection rate information in the region can help in understanding its epidemiological aspects. We review published articles on parvovirus infection in the current systematic review to estimate more accurately the prevalence rate of human parvovirus B19V infection in Nigeria.

## MATERIALS AND METHODS

We performed this analysis following the guidelines of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses), which provide evidence-based recommendations for conducting and reporting systematic reviews and meta-analyses [11].

### Literature Search Strategy

An in-depth literature search was carried out on articles published on Google Scholars, PubMed, Web of science, African Journals OnLine (AJOL), grey literature and cross checking of references of studies that resulted through the search of databases pertaining to Human Parvovirus B19 in Nigeria from 1 January 2009 to 20 March 2021. Our search strategy applied the following key words: ("prevalence" OR "Seroprevalence" OR "occurrence" OR "frequency") AND ("cross-sectional", OR "survey"), AND ("parvovirus", OR "B19V"), AND ("Nigeria", OR "north-central", OR "north-east", OR "north-west", OR "south-east", OR "south-south", OR "south-west", OR "37 states of the Nigerian federation").

### Inclusion and Exclusion Criteria

A study was considered eligible if: [i] epidemiological (cross-sectional, or case-control in design), [ii] published in English, [iii] conducted within Nigeria, [iv] accurate sample size and cases were clearly indicated, and [v] method of detection was reported. Exclusion criteria were as follows: [i] studies were not deemed eligible if devised as case reports, case-series, reviews or systematic reviews, [ii] published as conferences abstracts or in proceedings, [iii] not carried out in Nigeria, [iv] with overlapping/duplicate data and finally, [v] studies that did not report outcomes were excluded from the study since they did not have enough information for evaluation

**Outcome Measurement**

The primary outcome in our review is the prevalence of parvovirus B19V in different populations in Nigeria. The prevalence was calculated by dividing the number of patients with parvovirus infections by the total number of participants multiplied by 100

**Quality Assessment of the Studies and Data Extraction**

To evaluate the quality of included studies, we used the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Studies Reporting Prevalence Data [12]. The aim of this evaluation is to evaluate the methodological quality of a study and to determine the degree to which the study addressed the potential of bias in its design, conduct and analysis. The following items were used to assess the quality of the studies: (1) appropriate sample frame; (2) appropriate sampling technique; (3) adequacy of sample size; (4) description of study subjects and setting; (5) sufficient coverage of data analysis; (6) validity of method for identification of condition; (7) standard, reliable measurement for all participants; (8) appropriateness of statistical analysis; and (9) adequacy and management of response rate. This assessment was carried out independently by the authors and differences were addressed between authors during the quality assessment until a consensus was reached. Selection and assessment of studies quality were made independently, and disagreements during this process were discussed between the authors until a consensus was reached. We considered that the studies with scores from 0 to 3, 4 to 6 and 7 to 9 presented low, moderate and high quality. All the studies were included regardless the quality.

Data were extracted by the authors using a standardized data extraction checklist on excel spreadsheet. Extracted data included the surname of the first author, year of publication, study region, State, sample size, and number of positive cases.

**Statistical Analysis**

Considering the heterogeneity expected between the studies, all of the analyses were performed using the Der Simonian and Laird random-effects models [13]. Heterogeneity was assessed using the $I^2$ statistic [14]. The following values of $I^2$ are considered to be evidence of mild, moderate, and high heterogeneity between studies: 25–50%, 51–75% and > 75%, respectively. In addition, we investigated potential sources of heterogeneity by organizing groups of studies according to potentially relevant characteristics (subgroups) and by meta-regression analysis. To examine the publication bias, we used tests to detect asymmetry in the funnel plot proposed by Egger et al. [15]. We used the trim-and-fill method to account for any publication bias, predicated on the premise that the effect sizes of all studies are always typically distributed around the center of the funnel plot [16]. The meta-analysis was conducted using the meta package in R (version 4.0.0, R Statistical Computing Foundation, Vienna, Australia). Finally, $P < 0.05$ was considered statistically significant for all analyses.

## RESULTS AND DISCUSSION

**Search and Eligible Studies**

The literature search of four databases (PubMed, AJOL, Google Scholar and Web of Science) and reference screening yielded 118 articles. Following the title and the abstract review, on the grounds of duplicate, we excluded 82 of the studies. For eligibility for the next stage, we evaluated 36 full-text articles. Due to different reasons (Nonrelevant articles, and articles with inadequate data), we removed 12 of the studies. Subsequently, a total of 24 full-text articles were included in the meta-analysis (Fig. 1)

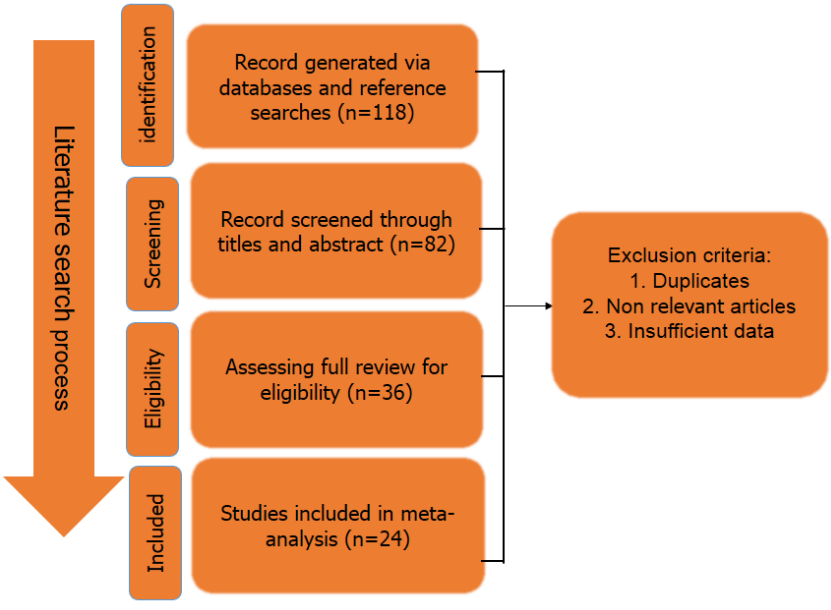


Figure 1: PRISMA Flow Diagram of Included Studies in the Systematic Review and Meta-Analysis on the Prevalence of Human Parvovirus B19 Infection in Nigeria

**Table 1: Summary Information from 24 Prevalence Studies of Human Parvovirus B19 Conducted in Nigeria between 2009 and 2020**

| Authors | Geopolitical zone/State | Study Population | B19V Diagnosis | Cases/ Sample Size (%) | Year of publica-tion | Quality |
|---|---|---|---|---|---|---|
| Emiasegen | NC/Plateau | Pregnant women | IgG & IgM | 111/273 | 2011 | High |
| Awolesi | SW/Ogun | Blood donors | IgM | 13/183 | 2020 | Low |
| Okojokwu | NC/Abuja | Pregnant women | IgG & IgM | 202/326 | 2018 | Low |
| Iheanacho | SW/Lagos | Blood donors & sickle cell | IgG & IgM | 201/300 | 2014 | Moderate |
| Ujo | NW/Kaduna | Sickle cell | IgG | 204/239 | 2012 | Low |
| Iyanda | SW/Oyo | Pregnant women | IgG & IgM | 55/231 | 2013 | Low |
| Ashaka | NC/Kwara | Anaemic children | IgM | 17/57 | 2018 | Moderate |
| Ajagbe | SW/Oyo | Anaemic children | IgM | 17/116 | 2018 | Moderate |
| Iwalokun | SW/Lagos | Sickle cell disease patients | IgG, IgM & DNA | 58/73 | 2013 | Moderate |
| Jegede | NW/Kano | Sickle cell, pregnant women | IgG | 191/460 | 2014 | Low |
| Ashaka | SW/Lagos | HIV patients | DNA | 13/200 | 2020 | High |
| Aleru | SW/Oyo | HIV patients | DNA | 2/158 | 2018 | High |
| Opaleye | SW/Osun | Hepatitis patients | IgG, IgM & DNA | 8/76 | 2011 | Moderate |
| Moses- | NC/Plateau | Sickle cell disease patients | IgG | 80/300 | 2019 | Low |
| Otutu | NC/Kogi | Blood donors | IgG & IgM | 37/88 | 2013 | Low |
| Musa | NC/Plateau | Sickle cell disease patients | IgG & IgM | 79/200 | 2010 | Moderate |
| Alao | NE/Borno | Sickle cell disease patients | IgG & IgM | 21/45 | 2013 | Low |
| Bukar | SW/Oyo | Pregnant women | IgM | 5/185 | 2018 | Moderate |
| Kolawole | SW/Lagos | Sickle cell disease patients | Serology | 10/68 | 2017 | Low |
| Ayolabi | SW/Lagos | Sickle cell disease patients | IgG & IgM | 38/67 | 2014 | Moderate |
| Iheanacho | NC/Abuja | Pregnant women | IgG & IgM | 57/200 | 2020 | Moderate |
| Abdullahi | SW/Lagos | Pregnant women | IgM | 35/93 | 2017 | Low |
| Ayolabi | NC/Nassarawa | Pregnant women | IgG & IgM | 111/273 | 2012 | Low |
| Akyala Iwalokun | SW/Lagos | Sickle cell disease patients | IgG & IgM | 8/64 | 2012 | Moderate |

Note: NC-North Central, NE-North East, NW-North West, SW-South West, SS-South South, IgG-Immunoglobulin G, IgM-Immunoglobulin M, DNA-Deoxyribonucleic acid

**Characteristics of Eligible Studies**

In total, 24 publications reporting on a total of 1463 cases of parvovirus B19 infection from 4475 participants across 12 States of Nigeria were reported between 2009 and 2020. Of the total 24 publications reviewed, 54.2% (13/24) and 33.3% (8/24) were from the southwest zone and north central zone respectively. The proportion of studies that were carried out in the northwest, north east and south south and south east of the country was 8%, 4%, 4% and 0% respectively. By State the distribution of studies was as follows: Lagos (29.1%; 7/24), Oyo (16.7%; 4/24), Plateau (12.5%; 3/24), Abuja (8.3%; 2/24), Ogun, Kaduna, Kwara, Kano, Osun, Kogi Edo, Borno and Nasarawa (4.2%; 1/24). The population targeted were sickle cell patients (41.6%; 10/24), pregnant women (37.5%; 9/24), blood donor (12.5%; 3/24), children, HIV patients (8.3%; 2/24), Hepatitis positive patient (4.2%;1/24), sickle cell and pregnant women combined (4.2%; 1/24). The main methods of diagnosis included serology (87.5%; 23/24) and molecular method (8.3%; 2/24), while a small proportion used serology and molecular combined (8.3%; 2/24). We found eleven (45.8%), ten (41.6%) and three (12.5%) studies with low, moderate and high quality respectively (Table 1)

**Overall Pooled Prevalence of Human Parvovirus B19 Infection in Nigeria**

The overall estimates of B19V infection in Nigeria was 26.6(19.8; 34.8) using the random-effects model. The $I^2$ statistic (96.3%, $P < 0.0001$) indicated substantial heterogeneity among the studies (Fig. 3).

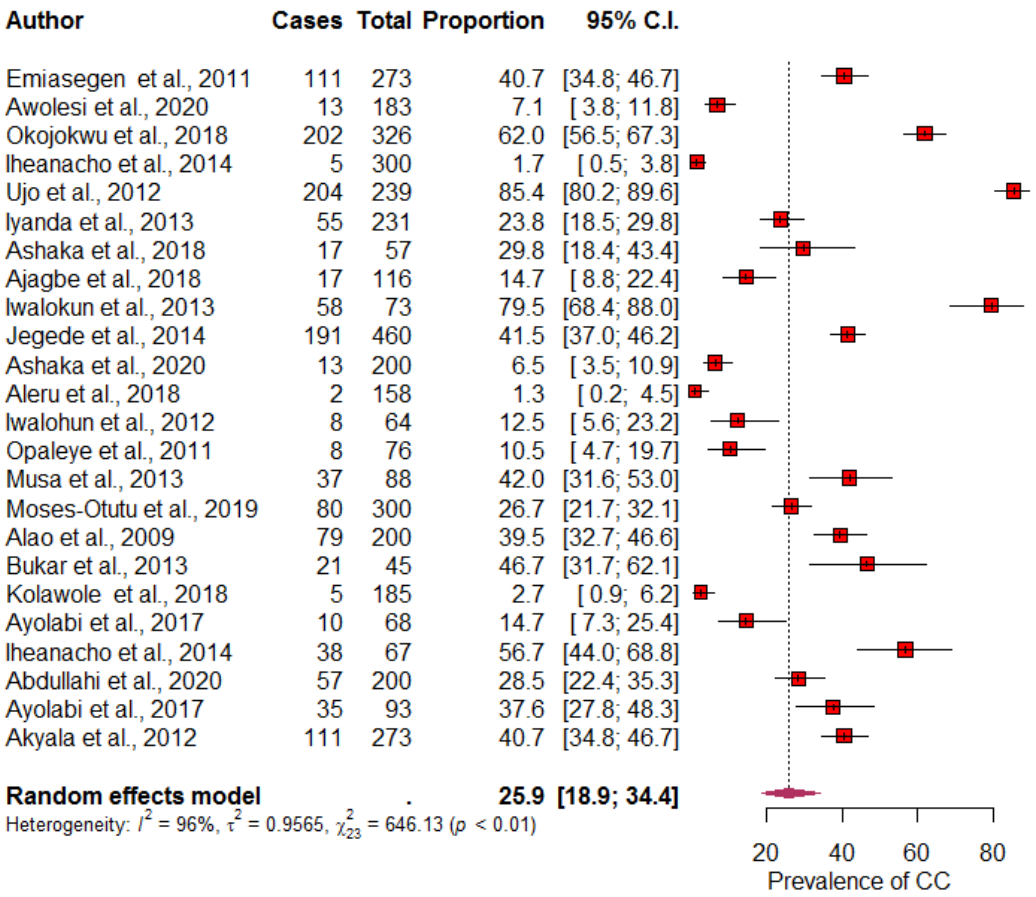


Figure 2: Forest plot diagram showing the estimated pooled prevalence of human parvovirus B19 infection in Nigeria between 2009 and 2024. Note: The area of each square is proportional to the study's weight in the meta-analysis, and each line represents the confidence interval around the estimate. The diamond represents the pooled estimate

**Sub-Group Analysis and Meta-Regression**

Since this meta-analysis exhibited a considerable heterogeneity, subgroup analysis was done In the subgroup analyses (Table 2), B19V prevalence was estimated to be 66.9% (20.5-94.0), 46.7% (32.8-51.1), 40.6% (31.9-49.9), 26.7% (22.0-32.0) and 13.5% (6.8-25.0) in the North west, north east, north central, south south and south west of Nigeria respectively. Studies conducted on sickle cell patients accounted for the highest prevalence 35.8% (20.7-54.4) followed by studies conducted on pregnant women 32.5% (23.4-43.0). Concerning diagnostic techniques, a higher prevalence of 31.4% (23.8-40.0) was reported in studies conducted using serological compared to molecular method 5.4% (2.2-12.7). By State (the prevalence of B19V were significantly (< 0.0001) as follows: Kaduna (85.4% CI 80.3; 89.3). Borno (46.7% CI 32.8; 61.1), Abuja (44.7% CI 16.9; 76.3), Kogi (42.1% CI 32.2; 52.6), Kano (41.5% CI 37.1; 46.1), Nassarawa (40.7 CI 34.9; 46.6), Plateau (40.2% CI 35.8; 44.7), Kwara (29.8% CI 19.4; 42.8), Edo (26.7% CI 21.9; 31.9), Lagos (21.3 CI 7.3; 48.0), Osun (10.5 CI 5.4; 0.19.7), Oyo (7.1% CI 2.3; 19.8), and Ogun (7.1%CI 4.1;11.9). (Fig 2) showed that the categorical variables: regions (p= 0.0002), State (p=0.0001), target population (p= 0.0136), publication year (p= 0.0001) and methods of diagnosis (p= 0.0001), were significantly associated with human parvovirus B19 prevalence in Nigeria. Measure by $R^2$, the following variables: regions = 3.39%; target population= 22.01%, and diagnostic methods = 14.66%, accounted for the high heterogeneity observed in this study.

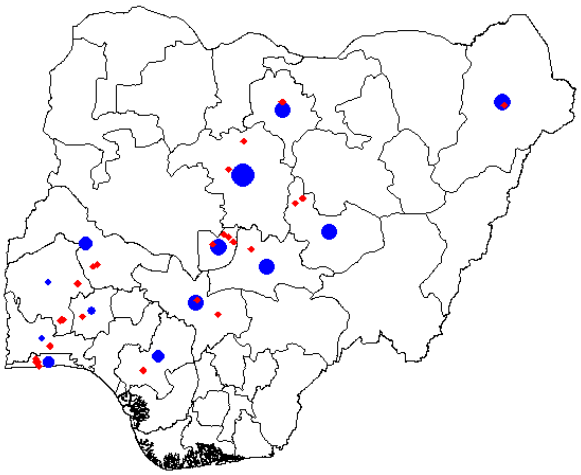

Figure 3: Map showing number of eligible studies (red) with states prevalence (blue) of human parvovirus B19 infection in Nigeria. Note red

**Table 2: Subgroup and Metaregression Analyses of Human Parvovirus B19 in Nigeria**

| Variable | NS | Cases/N | PP (95%CI) | Heterogeneity | | | Meta-regression | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Q | $I^2$ (%) | p-value | Coefficient (95% CI) | *p*-value | $R^2$ |
| Overall prevalence | 24 | 1377/4275 | 25.9 (18.9-34.4) | 646.13 | 96.4 | <0.0001 | | | |
| ***Region*** | | | | | | | | | |
| South-west | 13 | 267/2140 | 13.5[6.8-25.0] | 275.70 | 95.6 | < 0.0002* | -0.38 [-1.12;0.30] | 0.0005* | 3.39 |
| North-central | 7 | 614/1091 | 40.6[31.9-49.9] | 68.21 | 91.2 | | | | |
| North-west | 2 | 395/699 | 66.9[20.5-94.0] | 104.46 | 99.0 | | | | |
| North –East | 1 | 21/45 | 46.7[32.8-51.1] | 0.00 | - | | | | |
| South-south | 1 | 80/300 | 26.7[22.0-32.0] | 0.00 | - | | | | |
| ***Study period*** | | | | | | | | | |
| 2009 | 1 | 79/200 | 39.5[32.9-46.4] | 0.00 | - | 0.0001* | -0.09 [-0.21-0.02] | 0.1298 | 0.00 |
| 2010 | 1 | 86/200 | 2.7[1.1-6.3] | 48.24 | 97.9 | | | | |
| 2011 | 2 | 119/349 | 22.7[4.9-62.3] | 20.04 | 95.0 | | | | |
| 2012 | 3 | 323/586 | 45.9 [12.5-83.5] | 126.81 | 98.4 | | | | |
| 2013 | 4 | 171/437 | 47.9 [25.0-71.7] | 61.46 | 95.1 | | | | |
| 2014 | 3 | 234/827 | 21.2 [5.1-57.5] | 74.25 | 97.3 | | | | |
| 2017 | 2 | 45/161 | 24.9 [8.9-53.1] | 9.63 | 89.6 | | | | |
| 2018 | 4 | | 18.2 [4.7-51.0] | 109.10 | 97.3 | | | | |
| 2019 | 1 | 80/300 | 26.8 [21.9-31.9] | 0.00 | - | | | | |
| 2020 | 3 | 83/583 | 11.6 [3.5-31.8] | 43.91 | 95.4 | | | | |
| ***Population*** | | | | | | | | | |
| *Pregnant women* | 8 | 767/2041 | 32.5[23.4-43.0] | 145.88 | 95.2 | 0.0136* | -1.42(-2.70--0.17) | 0.0001* | 22.01 |
| *Sickle cell* | 9 | 503/1356 | 34.8[17.7-57.0] | 303.01 | 97.4 | | | | |
| *Blood donors* | 2 | 50/271 | 19.2[2.6-68.3] | 39.11 | 97.4 | | | | |
| *HIV patients* | 2 | 15/358 | 3.3[0.7-14.8] | 4.85 | 79.4 | | | | |
| *Others* | 3 | 42/249 | 17.3[9.2-30.2] | 8.87 | 77.4 | | | | |
| ***Study quality*** | | | | | | | | | |
| *High* | 3 | 126/631 | 8.5[1.1; 042.7] | 78.99 | 97.5 | 0.0742 | -0.23(-3.48 - 0.99) | 0.030* | 0.00 |
| *Moderate* | 10 | 292/1338 | 20.4[10.7-35.6] | 207.14 | 95.7 | | | | |
| *Low* | 11 | 959/2306 | 37.3(25.8:50.4) | 317.84 | 96.9 | | | | |
| ***Methods*** | | | | | | | | | |
| Serology | 21 | 1354/3841 | 30.7[22.9-39.9] | 537.21 | 96.3 | <0.0001* | -2.92(-4.06--1.79) | 0.0007* | 14.66 |
| Molecular | 3 | 23/434 | 5.4[2.2-12.7] | 7.62 | 73.7 | | | | |

**Publication Bias and Sensitivity Analysis**

The funnel plots (Fig. 4) and the Egger's test (P = 0.01367), result indicated publication bias in our meta-analysis. We conducted a Duval and Tweedie nonparametric trim and fill analysis using the random effect model to account for publication bias. After adjustment, the final pooled prevalence of B19V in Nigeria after the trim and fill analysis was 41.5% (31.7 - 52.1) (Fig. 5).

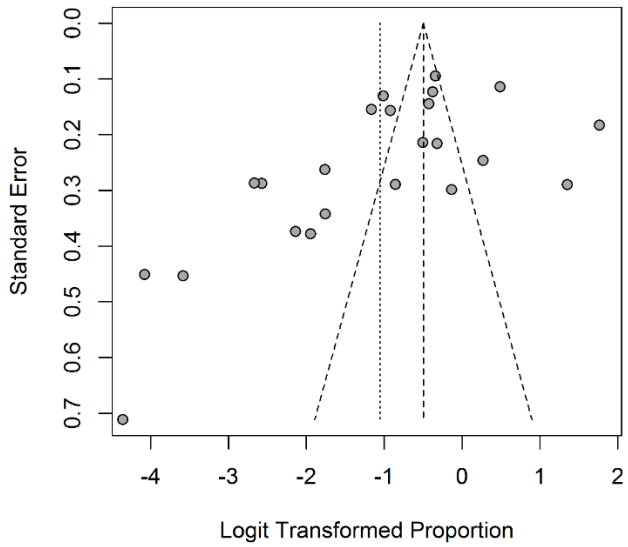


Figure 4: Funnel plot of human parvovirus infection in Nigeria. The figure displays the observed effect size of each study against the Standard Error of each study

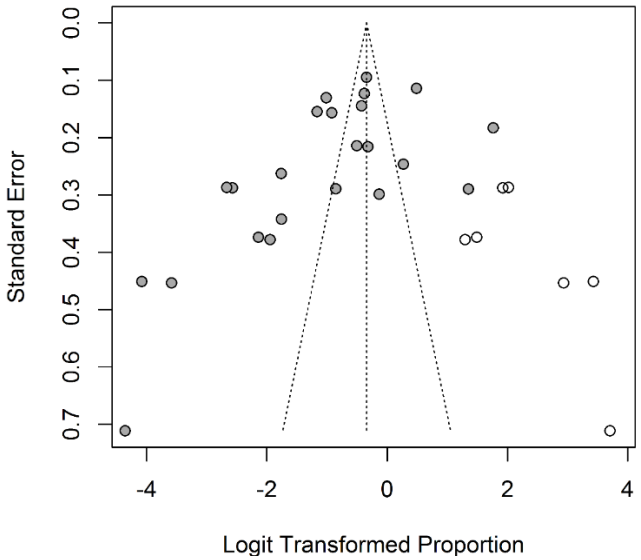


Figure 5: Funnel plot of human parvovirus B19 in Nigeria. The figure displays the observed effect size of each study against the Standard Error of each study. Note: Closed dots - indicate the observed studies, open dots- indicate the missing studies imputed by the trim and fill method

**Discussion**

One of the important causes of pure red cell aplasia and chronic anaemia in the immunocompromised host is parvovirus B19. Previous studies on this subject have been more restricted to specific groups and limited cities. The first estimate of human parvovirus B19 in Nigeria is the current systematic review and meta-analysis, which can be used to evaluate B19V prevalence in different parts of Nigeria and target groups.

Our analysis revealed that the prevalence of B19V was significantly different among regions and states in Nigeria. Varying socio-economic status, overcrowding, climatic conditions, geographical distribution of the different states, the time difference of study conducted and the immunological-haematological status of patients can be attributed to the variations observed [40]

With regard to the population studied, the prevalence observed in pregnant women in our review is higher and close to the prevalence reported in Nigeria [17, 38]. And since pregnant women have a 30% risk of transmitting the virus to their unborn babies leading to severe foetal morbidity and mortality [41], all pregnant women, especially those with anti-B19V IgM positive results and their foetuses should be closely monitored.

The prevalence of B19 in patients with sickle cell disease in this review is similar to that in Saudi Arabia [42], and lower than the prevalence reported by Obeid Mohamed among similar patients [43]. The increased frequency of blood transfusion and the nature of the tropism of red blood precursor cells can be associated to the presence of the virus in patients with sickle cell disease.

Although the pooled prevalence of B19V among blood donors documented in this review was significantly reduced compared to previous estimates in Nigeria [30], and mainland China [44] (Li et al., 2020), our study expressed concerns about rigid compliance to safe blood supply in blood and blood products recipients, particularly those who are immunocompromised (pregnant women, sickle cell disease patients children, and cancer patients). It also important to consider routine screening of blood donors for HPV-B19 to

prevent contaminated transfusion by relevant regulatory bodies such as the National Blood Transfusion Service (NBTS) and to intensify efforts to eliminate paid blood donations in the Nigerian health system.

The pooled prevalence of B19V among HIV-infected individuals in this study, although low compared to previous report [45] is a concern, as parvovirus B19 in addition to HIV has been shown to increase red destruction [45]. Similarly, the occurrence of B19V seen in children and positive hepatitis patients in our review has been documented by other researchers around the world [46-51]. B19V has been shown to play a potential role in the aetiology of liver disease, including fulminant liver failure, in hepatitis patients, while serious anaemia has been reported in children [29, 48].

The subgroup analysis showed significant heterogeneity between the different diagnostic methods used. Prevalence rates depend primarily on the tests used. Different commercial assays vary significantly in their performance with a wide range of specificities and sensitivities. However, as there is a lack of studies in Nigeria and Africa that demonstrate the sensitivity and specificity of the existing B19V diagnostic assays, further studies in this regard are recommended in Nigeria and Africa, where B19V is particularly prevalent in the at-risk group.

The current systematic review and meta-analysis is the first estimate of human parvovirus B19 in Nigeria. The following, however, are some of the limitations of this analysis. Firstly, although we have attempted our best to check all the B19V studies from the selected databases using several search terms, these searches may not have found all the relevant studies. Secondly, the majority of the studies included in our meta-analysis were not evenly distributed across regions, publication year, or target group. The uneven distribution of data may not reflect the true position of parvovirus B19 in Nigeria. However, these findings can, be used to assess the prevalence of parvovirus B19 in Nigeria.

## CONCLUSION

In conclusion, the prevalence of human parvovirus B19 was high and widespread in Nigeria, affecting various regions and target populations. We recommend that sickle cell patients, pregnant women, and blood donors be screened for infection on a regular basis as part of their routine clinical care.

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