HIV AND HUMAN PARVOVIRUS B19 CO-INFECTION: SEROPREVALENCE OF SERUM IgM and IgG SPECIFIC ANTIBODY AND ASSOCIATION WITH C D4+ T LYMPHOCYTES SUBSETS

[1]Adeno D, [1]Babadoko AA, [2]Musa BOP, [1]Yunusa RW, [3]El-fulaty, [1]Salifu A.
[1]Department of Haematology & Blood Transfusion, Ahmadu Bello University Zaria [2]Department of Medicine, Immunology Unit, Ahmadu Bello University Teaching Hospital, Shika – Zaria, Nigeria, [3]Department of Medical Laboratory Science, Ahmadu Bello University Zaria

Corresponding author:
David Adeno
Department of Haematology and Blood Transfusion
Ahmadu Bello University Teaching Hospital, Zaria
adenodavid@yahoo.com
DOI: https://doi.org/10.60787/njhaem-7-1-2-67

Keywords: Prevalence, HIV, Parvovirus B19, and CD4+ T-lymphocytes

ABSTRACT

Background: Parvovirus B19 (PV-B19) is a global and common infection in the general population, it is more frequently associated with immunosuppression including HIV infection. It causes anaemia in HIV infections, fifth disease, arthritis and arthralgia. Thus, we hypothesize the seroprevalence of PV-B19 is higher in HIV-positive individuals than those that are HIV-negative. The objective of this study was to determine and compare the prevalence of PV-B19 specific antibodies with the level of immunosuppression between the HIV positive and negative individuals in our locality.

Materials and Methods: A cross-sectional comparative study of consecutively enrolled, 92 HIV infected, treatment naive adults and 92 HIV-uninfected controls. Their sera were analysed for PV-B19 antibodies using recombinant PV-B19 specific IgM and IgG ELISA kit, while $CD4^+$T-cells was evaluated using Partec flow cytometer. The seroprevalence and CD4+ T cell counts of the HIV positive was compare with the HIV negative using Chi square test and Odds ratio. All statistical analysis was performed with SPSS software version 20 and a p-value of ≤ 0.05 was considered significant.

Results: The prevalence of PV-B19 IgM and IgG antibodies in HIV positive group were 28.8% (26 of 92) and 52.2% (48 of 92), respectively and those in the control group were 15.2% (14 of 92) and 32.6% (30 of 92) respectively, both were statistically significant $p < 0.05$. The $CD4^+$ T-cell count of the controls was significantly ($P < 0.001$) higher than that of the HIV positive group, however, this was not significantly (p=0.726) associated with PV-B19 IgM and IgG antibodies.

Conclusion: Human PV-B19 infection is common among treatment naïve HIV-infected adults however this may not be completely attributed to immunosuppression. Further studies are required to elucidate the mechanisms and significance of HAART, HIV viral load and PV- B19 DNA persistence, independently of the CD4+ cell status.

Keywords: HIV Infection, HAART naïve. Human PV-B19 IgM/IgG and $CD4^+$ T-cell count.

INTRODUCTION

Human Parvovirus B19 (PV-B19) is the only member of the family Parvoviridae known to be pathogenic in humans.[1] The virus is widespread, and manifestations of infection vary: In healthy immunocompetent individuals, it causes an exanthematic or joint disease, without haematologic involvement,[2] while in individuals with an underlying haemolytic disorder, it causes transient aplastic crisis. This may manifest as a persistent pure red cell aplasia or chronic anaemia in an immunocompromised host.[3,4] In the foetus, it causes hydrops fetalis, congenital anaemia and foetal death.[3,4] Parvo virus has a single-stranded DNA genome containing 5,596 nucleotides, an internal coding sequence flanked by the terminal repeat sequences.[5] The terminal sequences are palindromic and serve as primers for the synthesis of the complementary strand.[6] The most important viral proteins include the major NS1 and the capsid proteins VP1 and VP2.[7, 8]

About 3.5 million people are estimated to be living with HIV/AIDS in Nigeria and the estimated number of new infections and HIV/AIDS related deaths was 390,000 and 217,000 respectively in 2015.[9] In Kaduna state, Nigeria about 300,000 people of the over seven million population, are infected with HIV/AIDS, the highest in the North-west of Nigeria.[9] Infection with parvovirus B19 is global, the prevalence of IgG and IgM antibodies directed against B19 ranges from 2 to 15% in children 1 to 5 years old, 15 to 60% in children 6 to 19 years old, 30 to 60% in adults.[10] Among healthy individuals in Thailand, immunity to parvovirus B19 increases with age, with overall prevalence of PV-B19 infection being 63%[11] and 16 % among immunocompromised patients.[12]

In Ayingba and Lokoja in Kogi state of Nigeria, PV-B19 infections in blood donors revealed a seroprevalence of 42%.[13] A similar study among patients with sickle cell anaemia in North eastern Nigeria reported a seroprevalence of 42.2%.[14] A study of PV-B19 among children in Lagos aged 1-15 years reported a seroprevalence of about 56.7%. [15] On the other hand a study of PV-B19 infection among drug naïve and drug experienced seropositive HIV patient in Keffi, Nigeria reported a sero-prevalence of 62%,[16] while in Kano metropolis, Nigeria a prevalence of 51% was reported.[17] Ujo *et al.,* in a study of paediatric patients with SCA Zaria, a seroprevalence of 85.4% was reported.[18]

Parvo Virus-B19 infection induces a long-lasting antibody and cellular immune responses.[19, 20, 21] Acute infection is controlled by the neutralizing antibodies of the humoral immune response during the first week and as the viraemia declines in the second week, PV-B19 specific IgM develops.[22] In the natural course of the humoral immunity, PV-B19 specific IgM persist for several weeks to months and are substituted by PV-B19 specific IgG by the end of the second to early third week.[23] After natural infection, PV-B19 specific IgM begins to fall at the second month after the onset of illness, but may be present for several months. [23. 24] Virus specific IgA antibodies are also detected in about half of IgG-positive subjects[24] while PV-B19 specific antibodies of the IgE class have been detected in acute infection. [25,26]

Cell-mediated immunity is also developed during PV-B19 infection as demonstrated by Th1 and Th2 clonal proliferation in PV-B19 seropositive patients.[27] In patients with acute infection, vigorous cytokine production have been detected (IL-1, IL-6, IL-8 and TNF), some of which enhances production of all IgG subclasses (IgG1-4) in class-switched B-cells. [28, 29, 30, 31, 32] To date, both $CD8^+$ T cells with cytotoxic potential and $CD4^+$ T cells with helper functions have been described in PV-B19-seropositive individuals.[33] In HIV infection, patients with a CD4 count of > 350 cells/µl are capable of producing neutralizing antibodies, and persistent infections are more common among patients with advanced immunodeficiency.[33]

Diagnostic test for the virus is based on detection of specific IgM and IgG antibodies and DNA analysis using ELISA, PCR or Hybridization methods. [34] Effective treatments are feasible with commercial immune globulin and a protective vaccine is under development.[10] This study aims to assess the prevalence of PV-B19 serum specific IgM and IgG antibodies to human PV- B19 infection among treatment naïve HIV infected individuals in our locality and to determine the association of this antibodies to the degree of immunosuppression in HIV infected patients.

MATERIALS AND METHODS

This study was conducted in the Department of Medicine at Ahmadu Bello University Teaching Hospital (ABUTH) Zaria. Zaria is a major city in Kaduna State in North-western Nigeria, located in latitude 11°04'N 7°42'E as coordinates, having a total land area of 300km^2 and a population of 408,198.[35] It was a cross-sectional comparative study; participants comprised of 92 treatment naïve HIV seropositive adults (study group) and 92 apparently healthy HIV seronegative blood donors, students, hospital staff and patient relatives (controls [age matched]).

Ethical consideration: Informed consent was sought and obtained from each participant and confidentiality was strictly maintained. All participants were aged 18 years and above. The subjects included in this study were not exposed to any antiretroviral agent/s. This study received the approval of the ethics committee of Health Research Ethical Committee of ABUTH Shika, Zaria (AABUTH/HREC/52/2015) which is in accordance with the Code of Ethics of World Medical Association (Declaration of Helsinki involving use and handling of human subjects). .

Collection of data: Sociodemographic data included age, sex, ethnic group, religion, educational status and profession/occupation; biological data from the participants included omplete blood counts, CD4+ T lymphocytes counts, PV-B19 IgM and IgG serological status. All these data were collected using an interviewer-administered, semi-structured questionnaire.

Sampling, conservation and transport of samples: Five (5) mls of blood was collected from the participants at the phlebotomy unit, HIV treatment and care centre at ABUTH Zaria and blood donors at donor bay in Haematology and Blood Transfusion Services ABUTH Zaria. This was immediately aliquoted into 2.5mls K3 Ethylene Diamine Tetra Acetate anticoagulant and 2.5mls in plain specimen bottles (without anticoagulant) and transported in ice packs to the laboratory. Once in the laboratory, sera were obtained from the clotted plain bottles by centrifuging the sample at 3000 rpm for 5 minutes. The EDTA samples were analysed within six (6) hours of blood collection for complete blood and CD4+ T cells counts while sera were stored at -80°C ultra-low temperature Refrigerators and later used for detection of PV-B19 IgM and IgG antibodies.

Biological analyses: Complete blood count and $CD4^+$ T-cells were evaluated using automated haematology analyser (Swelab Alfa EN 591:2001) and Partec flow cytometer respectively. Serological analyzes were carried out at the Immunology laboratory of ABUTH Zaria of the Faculty of Medicine of the Ahmadu Bello University. PVB19 infection was investigated in all participants included in this study by the detection of

PVB19 IgM and IgG antibodies using the enzyme-linked immunosorbent assay (ELISA) with parvovirus B19 Sunlong kit, with sensitivity of 99% for both IgM /IgG and 100% specificity for both IgM and IgG according to information obtained from the manufacturer of the reagent (Sunlong Biotec Company LTD SL2654Hu China). All handling was carried out in accordance with the manufacturer's recommendations. Before interpreting the results, we calculated the average optical densities (OD) of the controls and ensured that it was within the range of values given on the manufacturer's data sheet. If the difference between two individual measurements was more than 20% compared to the mean OD of the controls, the test was to be resumed. The negative control should indicate an OD less than 0.3. Before the analysis, the test value of the blank reagent was deduced from all measured values. The OD thus obtained was located in the different rows (lower, doubtful, positive) of the column corresponding to the mean OD of the controls. The test was negative, doubtful or positive when this OD was in the corresponding range on the manufacturer's data sheet.

Results interpretation: Results for PV-B19 IgG and IgM were reported as either 'positive' or 'negative'. Results were interpreted as follows:

i. Positive IgM and negative IgG indicate acute/recent infection;
ii. Negative IgM positive IgG and indicate past infection;
iii. Positive IgM and positive IgG indicate infection within the last 7-120 days;
iv. Negative IgM and negative IgG indicate that the donor is not immune and that no evidence of acute/recent infection is identified.

Statistical analyses: The information collected was coded, stored and analysed in a database using Statistical Package for Social Science software *SPSS* (version 20) Chicago III USA, 2014. The database contains sample identification numbers, donor socio-demographic information and results of various serological tests. Data was processed and analysed; Quantitative variables were summarized using means ± standard deviation, medians (IQR), independent t-test and Mann-Whitney U-test for normal and non-normally distributed variables respectively as appropriate. The chi-square test was used to compare the seroprevalence of PV-B19 antibodies (IgM and IgG) between the study group (HIV-positive) and controls (HIV-negative). The odds ratio (OR) and its 95% confidence interval (95% CI) were used to evaluate the association between PVB19 infection and HIV infection. The value of $p \leq 0.05$ was considered statistically significant.

RESULTS

A total of 184 participants consisting of 92 HIV positive study group and 92 HIV-negative control group were studied. Data was tested for normality and results are presented as tables below.

Table 1 shows the general characteristics of the study population. The 28 to 37 age group was the most represented as HIV-positive study participants (26.4%) and 18 to 27 age group (21.3%) in the HIV-negative controls. Female were the most numerous with a male to female gender ratio of 1:1.97 for HIV-positive and 1:2.17 for HIV-

negative. The majority of the participants were of Hausa Ethnic group and represent 28.4% of HIV-positive participants and 22.4% were HIV-negative. In order to determine the seroprevalence of PV-B19 antibody, PV-B19 specific antibodies (IgM and IgG) were investigated in serum samples from 92 HIV-positive patients and 92 HIV-negative blood controls. As shown in Table 2, among the 92 HIV-positive samples tested for PV-B19 specific immunoglobulins, twenty-six (14.1%, OR 95% CI, 0.456 0.220, 0.943) were positive for IgM; forty-eight (26.1%, OR 95% CI, 0.444 0.244,0.806) was positive for IgG; eight (8%, OR 95% CI, 0.513 0.178,1.480) were positive for both antibodies and twenty six (26%, 95% CI, -1.8% - 12.4%) were negative for both subtypes.

Table 1: Socio-demographic Characteristics of the

Participants

Parameters	Study Group (%)	Control (%)	Total (%)	Statistical
Age (years)				
Mean (SD)	32.61±11.43	34.63±9.38	92	P = 0.543
Sex				
Male	31(16.8)	29(15.8)	60(32)6)	
Female	61(33.2)	63(34.2)	124(67.4)	$\varkappa^2$ = 0.099 p = 0.753
Total	92(50.0)	92(50.0)	184(100.0)	
Ethnicity				
Hausa	52(28.4)	41(22.4)	93(50.8)	
Yoruba	12(6.6)	18(9.8)	30(16.4)	
Igbo	4(1.6)	8(4.4)	11(6.0)	$\varkappa^2$ = 4.789 p = 0.188
Others	24(13.1)	25(13.7)	49(26.8)	
Total	92(49.7)	92(50.3)	184 (100)	

DISCUSSION

In this study, the ratio of the study to control groups was 1:1, although unmatched, the two groups come from the same population since their sociodemographic characteristics were not significantly different, when HIV-positive study group was compared to the control group (HIV-negative) table 1. However, there are more female participants than males in the study group. This could indicate that more females attended Nasara clinic (HIV clinic) than their males' counterpart due to various reasons such as avoidance of stigma and the responsibility of work in males, also female may have a more health seeking behaviour than the males.

The sero-prevalence of PV-B19 specific IgG antibody in HIV patients reported in this study is significantly higher than that of the HIV negative control group (52.1% Vs 36.2% p 0.007, OR 0.244, CI 0.806) but lower than 62% sero-prevalence reported in a study carried out in Keffi, Nasarawa State, Nigeria.[16] However, the sero-prevalence of PV-B19 specific IgG antibody in HIV negative control was lower than the prevalence of 85.4% reported among the paediatric age group from the same environment, Zaria.[18] The sero-prevalence of PV-B19 IgG antibody in this study is also lower than the 60-70% reported from England[36] but higher than 16.2% reported in Singapore[37], 39.5% reported in Jos[38] and 41.5% in Kano[19].

In this study, the sero-prevalence of PV-B19 specific IgM antibody in HIV patients is significantly higher than that of the HIV negative control group (28.8% Vs 15.2% p 0.032, OR 0.456, 95% CI 0.220, 0.943), which is indicative of recent infection because IgM antibodies is the first antibodies produced during humoral immune response and later substituted by IgG antibodies.[39] In HIV infected patients, PV-B19 specific IgG antibodies sometime persists, this suggest that chronic PV-B19 infection occurs in HIV infected patients whose immune system are not capable of mounting a sufficient response which agrees with the findings of Naides et al.,[20] who concluded that patients with HIV infection and in people with defective immune system, PV-B19 infection may often results in chronic infection. The higher PV-B19 IgM and IgG antibody observed in this work compared to the works of Yoto *et al*.,[40] may be due to difference in sampling methods, population size and assay method (DNA test in their case). Although the sero-prevalence of PV-B19 antibodies was significantly higher in the HIV positive patients, the sero-prevalence of both PV-B19 specific serum IgM and IgG (15.2% vs 28.8%) in the control group, implies that the prevalence of PV-B19 is also high even in the general population. This may not be unconnected to the influence of immunosuppression in HIV positive patients. The relatively high sero-prevalence among the healthy controls is consistent with reports from other studies in other part of the world, Heegard *et al*[41], in Copenhgen, Demark with B19 sero-prevalence range of 30-60% in healthy adults, 6.79% in China[42], 26% in Egypt[43], 27.96% in Pune[44], 63.3% in

Khartoum[45]. In Nigeria, a research conducted in Ayingba and Lokoja in Kogi state of PV-B19 infections in blood donors; a sero-prevalence of 42.0% PV-B19 for both IgG and IgM antibodies was reported[13], 56.7% in Lagos[15], 42.2% in North Eastern Nigeria,[14] but much more higher PV-B19 specific-IgG antibody sero-prevalence was obtained in blood donors; 74% in Belgium[46], 76.3% in Makkah[47],79.1% in Italy[48] and Vemazza et al[20]., found a significantly higher prevalence of B19-specific IgG in their cohort of HIV-infected patients than in a cohort of HIV-negative controls (81% vs. 57%, respectively; $P < 0.01$). Thus, our observations in this study are unexpected as different seroprevalence rates has been previously reported for selected groups of healthy individuals and patients with HIV infection. These variations in the rate of seropositivity among both the patients with HIV infection and healthy population might indicate an increased susceptibility to parvovirus B19 infection, or differences in the epidemiological and demographic characteristics resulting in different rates of exposure to co-infection with PV B-19. It may also be due to the differences in the specificity and sensitivity of the assay method used.

The relationship between human PV-B19 IgM and IgG status in both HIV treatment naïve study and control participants were also analysed (Tables 3 and 4), and both showed a significant relationship between IgG and IgM (p=0.009, p=0.015) respectively. Acute infection with PV-B19 is controlled by neutralizing antibodies of the humoral immune response, characterized by the appearance of serum IgM and IgG in the natural course of the infection. Antibodies directed at the unique portion of the linear B19 epitopes within the viral protein are functionally important as their ability to react correlates with their capacity to neutralize virus infectivity and patients with an underlying immunodeficiency and PV-B19 infection may have B19 specific antibodies that fail to recognize linear epitopes.[33, 49] Thus PV-B19 IgM and IgG status is associated with both acute and chronic infection, the virus is cytotoxic to host cells.[50]

The $CD4^+$ T-cells count of the healthy controls were significantly higher (P= 0.001) than that of the HIV infected patients (study group) which are immunocompromised compared to the former who are largely immunocompetent (Table 5). The low $CD4^+$ T-cells count of the study group is due to the destruction of $CD4^+$ T cells in HIV-infection which has been attributed to both direct infection and Fas/Fas ligand-mediated apoptosis.[51] Studies in HIV-infected patients have since shown a similar pattern of preferential and profound depletion of $CD4^+$ T cells within the systemic tract during infection.[52]

Following stratification of the level of CD4+ T count, the relationship between PV-B19 IgM and IgG status and $CD4^+$ T-cells count of the study and control group were studied, although a higher number of the participants had positive antibodies with severe immunosuppression (CD4+T cell < 350) and fewer number had CD4+T cell > 350, a trend towards increase seroprevalence rates that paralleled a declining CD4+ T lymphocyte count was observed. However, this trend was not significant when analysed with the use of *X2* test (PV-B19 IgM and IgG with $CD4^+$ T cell count of HIV infected positive patients and negative controls p=0.677, p=0.783 respectively Figure 1). Therefore, this implies that infection with PV-B19 may not necessarily be related to the degree of immunosuppression. Our finding is similar to the report of Petrol et al who reported a significantly higher prevalence of IgG antibodies to B19 in the HIV-positive group than among the controls (81% vs. 57%; $P < .01$, *X2* test).[53] IgM antibody is the first immune response that appears in order to neutralize the virus but do not last for a long period of time and therefore may not affect the $CD4^+$ T-cells at this initial stage of the infection. However, IgG antibodies play a vital role in immune response to PV-B19 infection and when produced, persist for several months to years. It also forms memory against future attack, IgG is directed to VP1 and VP2 conformation and to some extent VP1 linear epitope.[54] The virus replicates in human erythroid progenitor cells of the bone marrow and peripheral blood to inhibit erythropoiesis. It requires P-blood group antigen which is found mostly on cells of the erythroid lineage but also in platelets where it induces anaemia and thrombocytopaenia.[13, 55]

The prevalence of PV-B19 IgM and IgG positivity among the controls participants was assessed based on enrolment category Table 4). The result shows a relatively high percentage of PV-B19 infection in each of the five categories of the controls group, however though there was no significant difference between the categories (IgM p=0.476, IgG p=0.751). This implied, that blood donors, hospital staff, patients relative, student and every other person are at risk of Parvovirus B19 infection, and this agrees with the finding of other studies.[56, 57] Transmission of PV-B19 infection occurs via the respiratory route, through blood-derived products administered parentally and vertically from mother to foetus. Parvovirus B19-specific DNA has been detected in respiratory secretions, suggesting that virus is generally spread in the community by a respiratory route. Nosocomial transmission has been reported, and transmission has also been reported among staff in laboratories handling native virus. [58, 59]

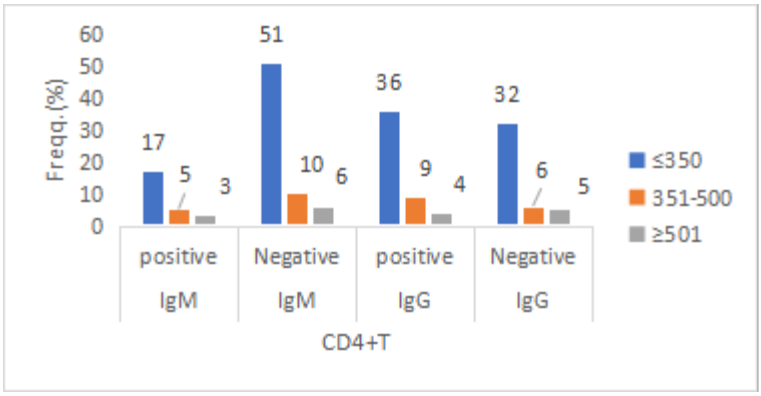
CONCLUSION

Parvovirus B19 infection is higher in treatment naïve HIV infected adult patients than HIV negative individuals and this may not be necessarily associated with the severity of immunosuppression. Thus, we advise a high index of suspicion both the general population and HIV infected individuals irrespective of the immunological stage of the disease.

Table 3: Relationship between PV-B19 IgM and IgG positivity among the participants

PV-B19 IgM	PV-B19 IgG					
	Study Group			Control		
	Positive (%)	Negative (%)	Total (%)	Positive (%)	Negative (%)	Total (%)
Positive	8(8.7)	18(19.6)	26(28.3)	9(9.8)	5(5.4)	14(15.2)
Negative	40(43.5)	26(28.3)	66(71.7)	21(22.8)	57(62.0)	78(84.8)
Total	48(52.2)	44(47.8)	92(100.0)	30(32.6)	62(67.4)	92(100.0)

Statistics:-Chi-square test;
Study Participants $\varkappa^2 = 6.655$, df = 1, p = 0.009*, OR=0.288 (95% CI: 0.110-0.761)
Control $\varkappa^2 = 5.936$, df = 1, p = 0.015, OR=4.89 (95% CI: 1.468-16.2)



Study group p=0.677 Controls p=0.783

Figure 1. Histogram showing the association of PV-IgM and IgG status with CD4$^+$ T-Lymphocytes Subsets in the Study Participants

CD4$^+$T Cells Reference range (≤350,350-500, ≤ 500 cells/µl).
FMO, Nigeria, 2014.

Table 4: Distribution of PV-IgM and IgG status among the controls

Category	PV-IgM			PV-IgG		
	Positive(%)	Negative(%)	Total (%)	Positive(%)	Negative(%)	Total (%)
Blood donors	3(3.3)	24(26.1)	27(29.3)	8(8.7)	19(20.7)	27(29.3)
Hospital Staff	7(7.6)	21(22.8)	28(30.4)	10(10.9)	18(19.6)	28(30.4)
Non-Hospital Staff	4(4.4)	33(35.9)	37(40.2)	12(13.0)	25(27.2)	27(40.2)

Statistics;
Chi-square test. $\varkappa^2 = 3.510$, df = 4, p = 0.476 (PV-IgM),
Chi-square test.$\varkappa^2 = 1.916$, df = 4, p = 0.751 (PV-IgG)

REFERENCES

1. Cossart Y E, Tsou C, Parker R A, Chorba T L, Wulff H, Tattersall P. Detection of antibodies and antigens of human parvovirus B19. *J. Clin. Microbiol*. 1974;24:522–526.
2. Pattison JR, Jones SE, Hodgson J, Davis LR, White JM, Stroud CE, Murtaza L. Parvovirus infections and hypoplastic crisis in sickle-cell anaemia. *Lancet.* 1981 Mar 21;1(8221):664-5.
3. Pedranti MS, Barbero P, Wolff C, Ghietto LM, Zapata M et al. Infection and immunity for human parvovirus B19 in patients with febrile exanthema. *Epidemiol Infect*. 2012;140:454–461.
4. Bowman CA, Cohen BJ, Norfolk DR, Lacey CJ. Red cell aplasia associated with human parvovirus B19 and HIV infection: failure to respond clinically to intravenous. *AIDS.* 1990;4(10):1038-9.
5. Deiss V, Tratschin JD, Weitz M, Siegl G. Cloning of the human parvovirus B19 genome and structural analysis of its palindromic termini. *Virology.* 1990;175(1):247-54.
6. Mitchell SA, Welch JM, Weston-Smith S, Nicholson F, Bradbeer CS. Parvovirus infection and anaemia in a patient with AIDS: case report. *Genitourin Med*. 1990;66(2):95-6.
7. Luo W, Astell CR. A novel protein encoded by small RNAs of parvovirus B19. *Virology.* 1993;195(2):448-55.
8. Kaplan C, Morinet F, Cartron J. Virus-induced autoimmune thrombocytopenia and neutropenia. *Semin Hematol.* 1992;29(1):34-44.
9. WHO. Global summary of the AIDS Epidemic December (2015). also available at *URL//www.unaids.org/epi/*2015.
10. Schwarz TF, Gürtler LG, Zoulek G, Deinhardt F, Roggendorf M. Seroprevalence of human parvovirus B19 infection in Sao Tomé and Principe, Malawi and Mascarene Islands. *Zentralbl Bakteriol*. 1989;271(2):231-6.
11. Poovorawan Y, Theamboonlers A, Suandork P, Hirsch P. Prevalence of antibodies to parvovirus B 19 in Thailand. *Southeast Asian J Trop Med Public Health.* 2000;31(2):422-4.
12. Suandork IN, Buleke MM. The prevalence of antibodies to human parvovirus B19 in Thailand. *J Med Microbiol*. 2000;25:151-3.
13. Musa SAU, Banwat EB, Zhakom P, Rumji EM, Yakubu RK, Rufai OA. Risk of Transfusion-Transmitted Human Parvovirus B19 Infection in Anyigba and Lokoja, Kogi State – Nigeria. *Iosr J Pharmacy.* 2013;3(3):66-70
14. Bukar AA. Seroprevalence fo parvovirus B19 and its clinical effects among anaemic SCA patients. *AJSIR* 4,2,195-200.
15. Oladipo OO. Prevalence of parvovirus B19 infections among children in Lagos, age 1-15 years. *Nig J of peadiat* 2007;34:79.
16. Amuta EU, Akyala A, Azua AT. Parvovirus B19 infection among drug naïve and drug experienced seropositive HIV patients. *Intern J of Academic Res*. 2013;5(2):102-106.
17. Jegede A, Aminu M, Ella EE. Seroprevalence of human parvovirus b19 among patients *African J of Clin Experimental Micro.* 2014;15(1): 21-26
18. Ujo H, Mamman AI, Aliyu A, Ogunrinde GO. The seroprevalence of parvovirus antibodies among children with sickle cell anaemia in Zaria. *African J of Clni Experimental. Microbiol*. 2012;13(2):74-78

19. Cohen BJ, Courouce AM, Schwarz,TF, Okochi,K. and Kurtzman,G.H. Laboratory infection with parvovirus B19. *J of Clin Pathol.* 1995;41:1027– 1028.
20. Naides SJ, Howard EJ, Swack NS. Parvovirus B19 infection in HIV-1 patients failing intolerant to Zidovidine therapy. *J of Infec Disea.* 1993;168:101-5
21. Anand A, Gray ES, Brown T, Clewley JP, Cohen BJ. Human Parvovirus infection in pregnancy and hydrops fetalis. *Engl J of Med.* 1987;316:183.
22. Benet JAG, Beard S, Cohen BJ, Alimenti A, Cantiniaux B, Levy J. Secondary infection with parvovirus Bl9 in an HIV positive patient. *Acquire immunodeficiency syndrome.* 2015;7:1131-1132.
23. Serjeant GR, Topley JM, Mason K, Serjeant BE, Pattison J, Jones SE. Outbreak of aplastic crises in sickle cell anaemia associated with Parvovirus-like agent. ***Lancet***. 1981;2(8247):595-7.
24. Lindblom A, Heyman M, Gustafsson I, Norbeck O, Kaldensjo T, Vernby A. Parvovirus B19 infection in children with acute lymphoblastic leukemia is associated with cytopenia resulting in prolonged interruptions of chemotherapy. ***Clin Infec Disease***. 2008;46(4):528-36.
25. Young NS. Hematologic and hematopoietic consequences of parvovirus B19 infection. ***Semi Hematol***, 1988;25:159.
26. Schneider E, Long SS, Pickering LK, Prober CG. Human Parvoviruses. In: ***Principle and Practice of Paediatric Infectious Disease.*** 4th edn. Philadelphia, PA: *Churchill Livingstone Elsevier*. 2012. 1087-1091.
27. Heegaard ED, Brown KE. Human parvovirus B19. *Clin Microbiol Rev.* 2002;15:485-505.
28. Kerr JR, Barah F, Mattey D. Circulating tumor necrosis factor-alpha and interferon gamma are detectable during acute and convalescent parvovirusB19 infection. *Engl J of Med*. 1995;321:51-60.
29. Nigro G, Bastianon V, Colloridi V, Ventriglia F, Gallo P. Human Parvovirus B19 infection in infancy associated with acute and chronic 93 lymphocytic myocarditis and high cytokine levels: Report of 3 cases and review. *Clin of Infect Dis.* 2000;31:65-69
30. Frickhofen N, Abkowitz J, Safford M. Persistent BI9 parvovirus infection in patients infected with human immunodeficiency virus type 1 (HIV-I): a treatable cause of anaemia in AIDS. *Ann Internal Med.* 1990;113:926-32
31. Takahashi Y, Murai C, Shibata S, Munakata Y, Ishii T. Human parvovirus B 19 as a causative agent for rheumatoid arthritis. *Proc Natl Acade Science USA.* 1998;95:8227-32.
32. Kawano Y, Noma T, Yata J. Regulation of human IgG subclass production by cytokines. *J of Immunol.* 1994;153:4948-58.
33. Kurtzman G, Frickhofen N, Kimball J, Jenkins DW, Nienhuis AW, Young NS. Pure red-cell aplasia of 10 years' duration due to persistent parvovirus B19 infection and its cure with immunoglobulin therapy. *New Eng J of Med* 1989;321:519-23.
34. Nacimento JP, Buckley M, Brown KE, Cohen BJ. The prevalence of antibody to human parvovirus B19 in Rio Janeiro, Brazil. *Revista do Instituto de Medicina Tropical de Sao Paulo*; 1990;32: 41-5.
35. Jamo IA. Democracy, Local Government and Infrastractural Development: A Study of Zaria Local Government in Kaduna State, Nigeria. International Journal of Education, Technology and Science. 2021;1(3):46–60.
36. Cohen BJ, Field AM, Gudnadottir S, Beard S, Barbara JA. Blood donor screening for parvovirus B19. *J of Virol Meth* 1998;30:233-238.
37. Matsunaga Y, Goh KT, Ubagawa E. Low prevalence of antibody to the human parvovirus B19 in Singapore. *Epidemiol infec* 1994;113(3):537-540.
38. Girei AI, Alao DE, Joseph DO. Damulak J. Haematological profile of Sickle Cell Cell Anaemia in Children with human parvovirus B19 infection in Jos, North Central Nigeria. *J of Med Research.* 1990;22:46-5.
39. Anderson A, Higgins PG, Davis LR, William JS, Jones SE, Kidd IM, Pattison JRD. Experimental parvoviral infection in humans. *J of Infec Dis.* 1985;152:257–265.
40. Yoto Y, Kudoh T, Haseyama K, Suzuki N, Oda, Chiba S. Incidence of Human Parvovirus B19 DNA Detection in Blood Donors. *BJH.* 2008;91(4):1017-1018.
41. Heegaard ED, Brown KE. Human parvovirus B19. *Clinical Microbiology Review* 2002;15:485-505.
42. Ou SH, Xie JZ, Zhang YL, Ni HY Song X. Prevalence of Parvovirus B19 Infection in Chinese Xiamen Area Blood Donors. *Zhongguo Shi Yan Xue Ye Xue Za Zhi* 2016;24:1572-1576.
43. Al-Danani D A-DH, Saudi M, Al-Shamahy H. Seroprevalence of parvovirus B19 IgG among blood donors in Aden, Yemen and Alexandria, Egypt. *J Chinese Clil Med* 2008;3:173-176.
44. Kishore J, Srivastava M, Choudhary N. Standardization of B19 IgG ELISA to study the seroepidemiology of parvovirus B19 in North Indian voluntary blood donors. *Asian J of Transfusion Science* 2010;4:86-90.
45. Amasi HO, Ayat J, Al-deen A. Seroprevalance of Human Parvovirus B19 among Blood

Donor Volunteers from Sudanese Blood Bank in Khartoum State. *J of ImmunoBiology* 2017; 2:3 DOI: 10.4172/2476-1966.
46. Letaief M, Vanham G, Boukef K, Yacoub S, Muylle L. Higher prevalence of parvovirus B19 in Belgian as compared to Tunisian blood donors: differential implications for prevention of transfusional transmission. *Transfusion science*. 1997;18:523-530.
47. Johargy AK. Seroprevalence of Erythrovirus B19 IgG among Saudi blood donors in Makkah, Saudi Arabia. *J of Family Community Med* 2009;16:111-114.
48. Manaresi E, Gallinella G, Morselli Labate AM, Zucchelli P, Zaccarelli D. Seroprevalence of IgG against conformational and linear capsid antigens of parvovirus B19 in Italian blood donors. *Epidemiol and infec.* 2004;132:857-862.
49. Söderlund M, Brown KE, Meurman O, Hedman K. Prokaryotic expression of a VP1 polypeptide antigen for diagnosis by a human parvovirus B19 antibody enzyme immunoassay. *J of Clin Microbiol* 1992;30:305-11.
50. Jianming Qiu,corresponding authora,* Maria Söderlund-Venermo,b,* and Neal S. Youngc. Human Parvoviruses. Clin Microbiol Rev. 2017;30(1): 43–113.
51. Li Q. Peak SIV replication in resting memory CD4+ T cells depletes gut lamina propria CD4+ T cells. *Nature.* 2005;434:1148–1152.
52. Gray JL, Bender BS, Quinn TC.. Haematologic abnormalities in the acquired immune syndrome. *American Journal of Medicine.* 1993;77:224-8.
53. Kapan JD, Schulte DJ, Feigin RD, Cherry JD. Demmler-Harrison, GJ, Kaplan SL. In: ***Feigin & Cherry's Textbook of Pediatric Infect Disea***. 1992. 6th ed. Philadelphia, PA: Saunders Elsevier; Vol 2: 1902-1920
54. **Cotmore SF, McKie LJ. Anderson CR. Astell and P. Tattersall.** Identification of the major structural and nonstructural proteins encoded by human parvovirus B19 and mapping of their genes by procaryotic expression of isolated genomic fragments. *J Virol.* 1986;60**:**548-557.
55. Evans JP, Rossiter MA, Kumaran TO, Marsh GW, and Mortimer PP. Human parvovirus aplasia: case due to cross infection in award. *British Med J. (Clinical. Research* Ed). 1984; (6418). 288:681
56. Koziol D, EG, Kurtzman J, Ayub NS, Young D. Nosocomial human parvovirus B19 infection: lack of transmission from a chronically infected patient to hospital staff. *Infect Control Hospital. Epidemiol*. 1992. 13:343–348. (Erratum, 13:511.
57. Miyamoto K, Ogami M, Takahashi Y, Mori T, Akimoto H, Terashita T. Outbreak of human parvovirus B19 in hospital workers. *J of Hospital Infect.2000.* 45:238-241
58. Cohen BJ, Courouce AM, Schwarz TF, Okochi,K, and Kurtzman GH. Laboratory infection with parvovirus B19. *J of Clin Path.*1988 41: 1027– 1028. 98
59. Shiraishi H, Sasaki M, Nakamura N, Yaegashi K, and Sugamura H. Laboratory infection with human parvovirus B19. *J of Infec*.1991 22:308–310