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Research Article

Molecular Detection of JC Polyomavirus among HIV Infected Patients in Ibadan, Nigeria.

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Abstract
JCV is associated with Progressive Multifocal Leukoencephalopathy (PML), a fatal demyelinating disease of the central nervous system which occurs majorly in patients with marked cellular immunodeficiency such as HIV/AIDS patients. Sub-Saharan Africa, including Nigeria, has the highest prevalence of HIV as well as HIV co-morbidities globally. Despite this, there is scanty information on the prevalence of JCV infection in Nigeria, especially among immunocompromised persons such as HIV infected individuals in the country. This study was therefore designed to determine the prevalence of JCV among ART naïve HIV infected individuals attending the ART clinic of the University College Hospital (UCH), Ibadan, Nigeria. Two hundred and forty plasma samples from 160 ART naïve HIV positive patients and 80 HIV negative individuals were tested for the presence of JCV by polymerase chain reaction and absolute CD4 count determined using flow-cytometer (Partec, Germany). Clinical and demographic data were also collected from each participant after obtaining their informed consent. Thirty-five (35) of the 160 (21.9%) ART naïve HIV infected individuals were positive for JCV DNA while only 5 (6.3%) of the 80 HIV negative individuals tested positive for JCV DNA. The rate of JCV infection was higher among males in both groups. Furthermore, it was observed that a high proportion of ART naïve HIV infected individuals with CD4+ T cell count >500cells/µl at baseline that were infected with JCV cleared the infection within six months post ART. Findings from this study show that JCV infection is common among HIV infected individuals in Nigeria.
Key Words: Progressive Multifocal Leucoencephalopathy (PML), JCV, Plasma, HIV/AIDS patients

INTRODUCTION

JC virus (JCV) is classified as a member of the polyomaviridae family which also includes BK virus (BKV) and SV40. JCV, as with all polyomaviruses, is composed of a small, non-enveloped, icosahedral virion with a supercoiled double-stranded DNA genome (Imperiale and Major, 2007). Serologic data suggest that exposure to JCV is widespread in the general population since seroprevalence rates varies from 70% in young adults to 100% in the elderly (Kitamura et al, 1990). Primary infection with JCV occurs via an oral or respiratory route without any known associated clinical manifestation, and the virus could persist lifelong in kidneys, with intermittent viral excretion in urine (Tavazzi et al., 2012).Recent data are reporting a protective association between JCV and chronic kidney disease (CKD) (Mubanga et al., 2019; Kruzel-Davila et al., 2021)

However, in patients with marked cellular immunodeficiency such as HIV infected patients, cancer patients, and organ transplant recipients, JCV can spread from the kidney to the central nervous system and causes a fatal, demyelinating disease, progressive multifocal leukoencephalopathy (PML). The prolonged immunosuppression associated with AIDS contributes to the high prevalence of PML among people living with HIV/AIDS, and was an extremely rare disorder prior to the AIDS pandemic (Delbue et al., 2012). The highest number of PML cases occurs in patients infected with HIV, reaching as high as 8% of all AIDS cases (Delbue et al., 2012). Although the use of highly active antiretroviral therapy (HAART) has reduced the number of opportunistic infections, PML remains a substantial neurologic complication in HIV-1/AIDS patients and it is currently the 3rd most common infectious neurological disease seen in HIV-1+ patients (Delbue et al., 2012). At present, there are no effective treatments for PML, making the prognosis of the disease very poor (Betrami and Gordon, 2014). Since majority of healthy adult are seropositive for JCV, serological assays are not very useful for diagnosing ongoing JCV associated diseases. Instead, JCV DNA detection in urine and blood have become pivotal laboratory assays in the management of immunodeficient patients.

To date, there is very scanty data on the burden of JCV among HIV infected and the general population in Nigeria as well as from other African countries. Hence, the study was designed to determine the prevalence of JCV infection among ART naïve HIV infected patients in Ibadan, Nigeria as well as determine JCV infection status among HIV/JCV co-infected patients six months post ART initiation.

MATERIALS AND METHODS

Study Population: The study was carried out among patients receiving care at the University College Hospital in Ibadan.

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Ibadan is a large metropolitan city that lies in the geographical coordinates of 10º23' 0"N, 12º 5' 0" E. It is the third most populous city in Nigeria and located in the Southwestern region of Nigeria with about 4 million people and a land area of 3,080km². The University College Hospital is the largest tertiary hospital in south-western Nigeria with a capacity of 850 bed spaces and 163 examination couches. Patients from different part of the country, especially neighbouring southwestern state patronises the hospital for care. Archived plasma samples from persons infected with HIV stored at -80°C in the Department of Virology, College of Medicine, University College Hospital, Ibadan were used for this study. They included 160 baseline (pre ART) blood samples collected from persons enrolled for ART between January and May, 2014 before ART initiation.

Individuals who were positive for JCV (HIV/JCV co-infected) were retested for the presence of JCV infection after commencement of anti-retroviral treatment for a minimum of six months. In addition, 80 HIV negative individuals were enrolled into the study as controls. Demographic information and clinical data of the patients were obtained from records of the Department of Virology for archived samples while a structured questionnaire was used to capture information from HIV negative control after obtaining their consent. Plasma were brought from freezer and allowed to thaw after which 1ml was transferred into fresh cryovials for DNA extraction. For the control group, plasma was separated from whole blood collected in EDTA-containing tubes by centrifugation at 1,400 r.c.f for 7 mins. The samples were subjected to DNA extraction immediately after separation. Viral DNA was extracted from 200uL samples of plasma using the guanidinium thiocyanate method.

Polymerase Chain Reaction for Detection of Polyomavirus DNA: The extracted DNA was used as a template for the detection of Polyomavirus DNA by amplification of a 173-bp of the large tumour antigen gene (TAg). A pair of 20-base oligomer primers (PEP-1 and PEP-2) complementary to the TAg region of polyomavirus genome was used (Arthur et al., 1989). The target region was amplified in a reaction with a final volume of 25µl containing 12.5µl PCR mix (Jena Biosciences®, Germany) - PCR buffer, MgCl2, dNTP and Taq polymerase; 1µl each of both forward and reverse primer, 7.5µl nuclease free water, and 3µl of template DNA. The sequences of the primers are shown in Table 1. The reaction mix was subjected for amplification in a Perkin Elmer PTC 200 thermocycler as follows: 40 cycles of 94 ºC for 1.5 minutes, 55 ºC for 1.5 minutes and 72 ºC for two minutes. An initial DNA denaturation step at 94 ºC for 10 minutes and a final extension step for seven minutes at 72 ºC were also included. The length of the obtained fragment from the amplified samples was 173 bp.

Polymerase Chain Reaction for Detection of JCV DNA: Polyomavirus DNA positive samples were subjected to another round of PCR for the detection of JCV infection using the original DNA extracts as templates and a set of primers specific for JCV T-antigen sequences (Table 1). PCR was performed in a total volume of 25µl with 12.5µl PCR mix (Jena Biosciences®, Germany) containing PCR buffer, MgCl2, dNTP and Taq polymerase; 1µl each of both forward and reverse primer, 5.5µl nuclease free water, and 5µl of template DNA. JCV positive and negative control samples were also included. The protocol described by Badri et al. (2017) was adopted with some modifications. The cycling conditions were as follows: 95 ºC for 8minutes for initial DNA denaturation followed by 35 cycles of 95 ºC for 30 seconds, 55 ºC for 30 seconds, and 72 ºC for 30 seconds and then 72 ºC for 7 minutes for a final extension step. The length of the amplified fragment was 181 bp. 5l of the PCR product was analyzed by gel electrophoresis in 2% Agarose, and stained with SYBR Green and the product was visualized by using Biorad® image reader (a UV Transilluminator). Expected band size of amplicons were 173bp for polyomavirus DNA (Figure 1), 181bp for JCV DNA (Figure 2). Collected data were analyzed using statistical package for social science (SPSS) version 20. Student's T-test was used to test significance between selected parameters of the study and p value of < 0.05 considered significant.

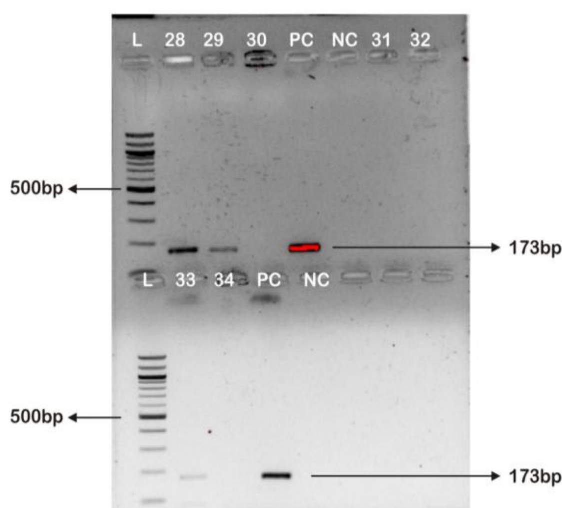

Figure 1
Detection of polyomavirus DNA TAg gene by PCR
Lanes 28, 29, and 33 were positive for JCV, while 31, 32 and 34 were negative. L=ladder, PC =positive control, NC=negative control. Expected base pair for polyomavirus =173bp

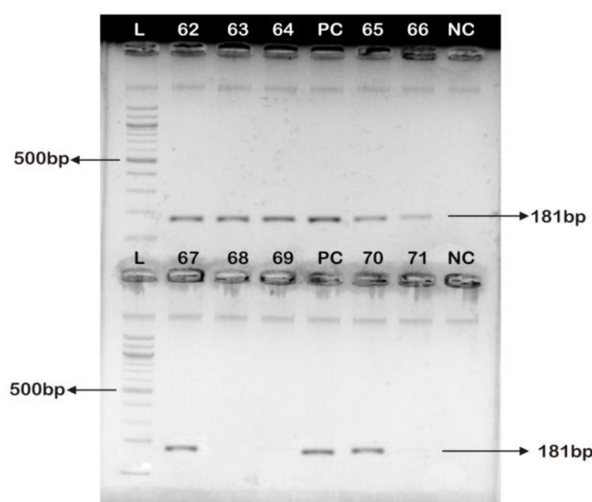

Figure 2
Detection of JCV DNA TAg gene by PCR
Lanes 62-66 and 67 were positive for JCV while 68 and 69 were negative. L=ladder, PC=positive control, NC=negative control. Expected base pair for JCV = 181bp

Table 1.
Nucleotide sequence of the primer pair for Polyomavirus and JCV DNA detection

Virus	Primers	Nucleotide Sequence (5'-3')	Region	Base pair (bp)
Polyomavirus	PEP-1 PEP-2	AGTCTTTAGGGTCTTCTACCGGTGCCAACCTATGAACAG	TAg	173
JCV	3049-3069 3229-3207	TGGCCTGTAAAGTTCTAGGCAGCAGAGTCAAGGGATTTACCTTC	TAg	181

Arthur et al. (1989); Badri et al. (2017).

RESULTS

Two hundred and forty participants comprising 156 females and 84 males were enrolled for this study. The mean age of the HIV infected individuals was 39.63 ±12.36 (range: 15-72years) while the mean age and standard deviation of the control group was 34.99 ±10.51 (ranged: 19 to 60 years). A total of 49 (30.6%) and 35(21.9%) of the 160 samples from ART-naïve HIV positive individuals were positive for polyomavirus and JCV DNA respectively as against 7(8.8%) and 5(6.3%) of the 80 control HIV negative individuals. A higher rate of JCV infection was found among males (27.8%, 10.0%) than in females (18.9%, 4.0%) in both case (p=0.197) and control (p=0.283) groups, although these differences were not significant (Table 2).

Table 3 shows the distribution of JCV infection by age among HIV positive and HIV negative individuals. The highest rate (41.7%) was found in those above 55 years old and lowest in the 15-24 age groups. The rate of JCV infection was highest among HIV infected individuals with CD4+ T cell count >500 CD4cells/μl in ART naïve patients (41.2%) while the lowest rate was found among those with CD4+ T cell count between 351-500 CD4cell/μl (13.6%) as shown in Figure 3 (p=0.022).

Table 4 shows the mean CD4 lymphocytes before and after ART initiation and JCV infection status among HIV/JCV co-infected patients. HIV/JCV co-infected patients with persistent JCV infection six months post ART initiation had mean CD4 counts of 161+53 cells/ul and 349+86 cells/ul while HIV/JCV co-infected individuals who cleared JCV six months post ART initiation had significantly higher mean CD4 counts of 267+90 cells/ul and 470+189 cells/ul before and six months post ART initiation respectively (p Value = 0.003, 0.011 respectively)

Table 2.
Distribution of JCV infection by gender among HIV positive and HIV negative individuals

	HIV Positive		HIV Negative (Controls		
GENDER	**Number Tested**	**Number (%) Positive**	**Number Tested**	**Number (%) Positive**	**Total**
Female	106	20 (18.9)	50	2 (4.0)	156
Male	54	15 (27.8)	30	3 (10.0)	84
Total	**160**	**35 (21.9)**	**80**	**5 (6.3)**	**240**

P= 0.197 (cases), p= 0.283 (control

Table 3.
Distribution of JCV infection by age among HIV positive and HIV negative individuals

	HIV Positive		HIV Negative		Total
AGE GROUP	**Number Tested**	**Number (%) Positive**	**Number Tested**	**Number (%) Positive**	**Tested (%+)**
15-24years	17	1 (5.9)	14	0 (0.0)	31(3.2)
25-34years	41	9 (22.0)	30	2 (6.7)	71 (15.5)
35-44years	43	9 (20.9)	21	1 (4.8)	64(15.6)
45-54years	40	8 (20.0)	10	0 (0.0)	50 (16.0)
≥55years	19	8 (42.1)	5	2 (40.0)	24 (41.7)
Total	**160**	**35 (21.9)**	**80**	**5 (6.3)**	**240 (16.6)**

p value= 0.104 (cases), p value= 0.022 (control), p value=0.0047 (Total)

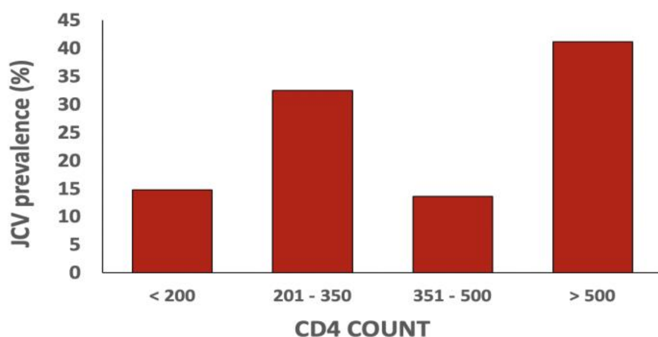

Figure 3.
Distribution of JCV infection by CD4^{+} cell counts among ART Naïve HIV infected individuals

Table 4:
Mean CD4 lymphocytes of HIV/JCV co-infected patients and JCV infection status six months post ART initiation

	Mean CD4 Lymphocytes (cells/ul)		
	ART Naïve	**Six Months Post ART**	**P-Value**
JCV Positive	161±53	349±86	0.003
JCV Negative	267±90	470±189	0.011

DISCUSSION

We found a JCV prevalence of 21.9% (35/160) among the ART naïve HIV infected cohort as against 6.3% JCV prevalence among HIV seronegative group; confirming earlier reports of an increased frequency of JCV among HIV infected patients (Karalic et al., Nali et al., 2012; Machado et al., 2011; Kruzel-Davila et al., 2021). Very few studies on JCV have been conducted in Nigeria and the African continent. Although the study population differs, the result of this study is higher than the rate of JCV (11.8%) reported by Samah et al. (2014) among patients with solid tumours in Egypt and among HIV infected individuals with or without CKD (18.8%) in Nigeria and Ghana (Kruzel-Davila et al., 2021). However, it should be noted that JCV viral load was quantified in urine samples in the study reported by Kruzel-Davila et al., 2021. This method may partly be responsible for the lower prevalence. Another reason for the lower prevalence may be the study population. Previous studies have associated a lower burden of CKD among JCV infected individuals (Nqebelele et al., 2019; Mubanga et al., 2019). Also, the prevalence detected in this study is low when compared to the 48% prevalence reported by Badri et al. (2017) among renal transplant patients in Sudan; this is expected as virions may enter the circulation through peri-tubular capillaries following tubular damage in renal transplant patients.

The result of this study is in agreement with the rate of 22.7% detected in the plasma of AIDS patients in France by Lafon and colleagues in 1998. The similarity in rates could be as a result of the similarity in gene sequence amplified (early region) and the fact that both studies demonstrated JCV in plasma samples (viremia) and not in urine (viruria) or CSF samples. In the same study by Lafon et al. (1998), JCV DNA rate of 40% and 56% was reported when CSF and urine samples were used respectively. Several studies have shown higher predictive rates of JCV DNA detection in urine, peripheral blood cells, and CSF samples of immunocompromised and immunocompetent individuals (Nali et al., 2012; Machado et al., 2011; Lafon et al., 1998; Dubois et al., 1998; Dubois et al., 1997). However, the prevalence of JCV DNA detected in this study sharply contrasts with a previous study conducted among HIV infected patients in France, where the prevalence was estimated at 40.3% (Dubois et al., 1997). The disparity in prevalence could be because the study by Dubois et al. (1997) detected JCV DNA in multiple samples (peripheral blood leucocytes and plasma) of HIV infected patients including those with confirmed progressive multifocal leukoencephalopathy (PML) while this study used only plasma samples of HIV infected patients.

A significant association was found between JCV DNA positivity and the degree of immunodeficiency as measured by the T CD4+ cell count (p= 0.022). The highest rate of JCV infection was obtained among ART naïve HIV infected individuals with CD4+ T-cell count >500 cells/µl. The high JCV prevalence in this group is quite interesting and supports the reports of Dorries et al. (2001) who earlier posited that infection with JCV is not related to the immunodeficiency status but by an unknown mechanism of persistence and reactivation among immunocompetent and immunocompromised individuals as well as Berger et al. (1998) who reported PML occurrence in persons with relatively high CD4+ T-cell count or suppressed viral replication. This finding albeit is in contrast with several other studies where the highest prevalence of JCV infections was among HIV infected individuals with CD4+ T-cell counts less than 200cells/µl (Karalic et al., 2014; Nali *et al*., 2012; Bossolasco et al., 2005; Dubois et al., 1997). However, it should be noted that a limitation of this study is our low sample size. While the rate of JCV was highest among individuals with CD4 >500 cells/µl, our data showed that those with persistent JCV infection after 6 months of ART had a relatively low baseline CD4 counts compared with those who became JCV negative months after ART. This further reiterates the idea that JCV infection may be associated with immune deficiency through a different mechanism. There may be need for further studies to elucidate this speculation.

The rate was highest (50%) among HIV positive individuals in the age group greater than 55years. This may be because waning of cellular immunity occurs with age causing higher reactivation of latent JC polyomavirus especially in immunocompromised individuals. There was no significant difference in the proportion of positive individuals in this cohort. This study reaffirms findings from other authors (Karalic et al., 2014; Nali et al., 2012; Knowles et al., 1999) who earlier reported that there is no association between JCV infection rate and age of immunocompromised HIV infected patients. We nevertheless, found an association between JCV rate and age in the HIV negative population (p= 0.022). JCV rate was highest among age group greater than 55 years. This increase has been reported for JCV among immunocompetent individuals by several authors, in which the older the population, the higher the rate of JCV infection (karalic et al., 2014; Polo et al., 2004; Kitamura et al., 1990). This could be due to T cell atrophy, concomitant decrease in immunity with age as well as immunosenescence.

PML associated with HIV-1 infection can be separated into two distinct phases; before and after the introduction of highly active anti-retroviral therapy (HAART). In the pre-HAART era, PML was considered an AIDS defining illness, affecting 7–10% of HIV-1 infected individuals (Berger and Concha 1995). In the era of HAART, an estimated 3–5% of AIDS patients developed PML (Major et al, 2010). We hypothesized that antiretroviral therapy may have an effect on JCV infection, hence we investigated the burden of JCV among infected individuals after six months of ART, out of the 15 persons investigated, 6(40%) were still infected with JCV. This high persistent rate recorded in our cohort is inline with findings of several authors (Antoniolli et al., 2017, Antinori et al. 2001; Luca et al., 2000) who earlier reported that not all HIV/JCV co-infected patients receive significant benefit from ART and the incidence of PML among HIV/AIDS patients has not decreased like other opportunistic infections even in the HAART era.

In conclusion, the findings from this study is in support of previous studies which reported high prevalence of JCV among HIV infected individuals. In addition, our data revealed

that HIV/JCV co-infected patients who successfully cleared JCV infection had significantly higher baseline CD4 counts than those with persistent JCV after ART initiation; thus highlighting the importance of a relatively preserved immune status for effective clearance of JCV infection among HIV/AIDS patients on ART.

REFERENCES

Antinori, A, Ammassari, A., Giancola, M.L., Cingolani, A., Grisetti, S. and Murri, R. (2001). Epidemiology and prognosis of AIDS associated progressive multifocal leukoencephalo-pathy in the HAART era. Journal of Neurovirology 7:323-328.

Antoniolli, L., Borges, R. and Goldani, L.Z. (2017). BK Virus Encephalitis in HIV-Infected Patients:Case Report and Review. Case Reports in Medicine 17: 1-6.

Arthur, R.R., Dagostin, S. and Shah, K.V. (1989). Detection of BK Virus and JC Virus in Urine and Brain Tissue by the Polymerase Chain Reaction. Journal of Clinical Microbiology 27 (6): 1174-1179.

Badri, A.M., Janay, A., Jonas, H., Liban, A.H., El Fadol, A.S.M., El Hussein, A.R.M., Elkhidir, I.M. and Enan, K.A. (2017). Molecular Detection of JCV in Urine and Blood Samples of Renal Transplant Patients in Khartoum State, Sudan. Molecular Biology 6 (1): 178-182.

Berger, J.R. (2003). Progressive multifocal leukoencephalopathy in acquired immunodeficiency syndrome: explaining the high incidence and disproportionate frequency of the illness relative to other immunosuppressive conditions. Journal of Neurovirology 9 (1): 38–41.

Berger, J.R., Levy, R.M., Flomenhoft, D. and Dobbs, M. (1998). Predictive factors for prolonged survival in acquired immunodeficiency syndrome-associated progressive multifocal leukoencephalopathy. Annals of Neurology 44: 341–349.

Berger, J.R. and Concha, M. (1995). Progressive multifocal leukoencephalopathy: the evolution of a disease once considered rare. Journal of Neurovirology 1: 5–18.

Bossolasco, S., Calori, G., Moretti, F., Boschini, A., Bertelli, D., Mena, M., Gerevini, S., Besteti, A., Pedale, R., Sala, S., Sala, S., Lazzarin, A. and Cinque, P. (2005). Prognostic Significance of JC Virus DNA Levelsin Cerebrospinal Fluid of Patients with HIV- Associated Progressive Multifocal Leukoencephalopathy. Clinical Infectious Diseases 40:738–44.

De Luca, A., Giancola, M.L., Ammassari, A., Grisetti, S., Paglia, M.G., Gentile, M., Cingollani, A., Murri, R., Liuzzi, G., Monfortte, A.D. and Antinorri, A. (2000). The Effect of Potent Antiretroviral Therapy and JC Virus Loadin Cerebrospinal Fluid on Clinical Outcome of Patients with AIDS-Associated Progressive Multifocal Leukoencephalopathy. The Journal of Infectious Diseases 182:1077–83.

Doerries, K. (2001). Latent and Persistent Polyomavirus Infection. In: Khalili, K., Stoner, G.L. (Eds.), Human Polyomaviruses: Molecular and Clinical Perspectives. Wiley-Liss, New York, pp. 197–235.

Dubois, V., Dutronc, H., Lafon, M.E., Poinsot, V., Pellegrin, J., Ragnaud, J., Ferrer, A. and Fleury, H.J.A. (1997). Latency and Reactivation of JC Virus in Peripheral Blood of Human Immunodeficiency Virus Type 1-Infected Patients. Journal of Clinical Microbiology 35 (9): 2288-2292.

Dubois, V., Moret, H., Lafon, M.E., Janvresse, C.B., Dussaiax, E., Icart, J., Karaterki, A., Ruffault, A., Taoufik, Y., Vignoli, C. and Ingrand, D. (1998). Prevalence of JC Virus viraemia in HIV-infectedpatients with or without neurological disorders: a prospective study. Journal of NeuroVirology 4:539-544.

Delbue, S., Elia, F., Carloni, C., Tavazzi, E., Marchioni, E., Carluccio, S., Signorini, L., Novati, S., Maserati, R., & Ferrante, P. (2012). JC virus load in cerebrospinal fluid and transcriptional control region rearrangements may predict the clinical course of progressive multifocal leukoencephalopathy. Journal of cellular physiology, 227(10), 3511–3517. https://doi.org/10.1002/jcp.24051.

Imperiale, M.J. and Major, E.O. (2007). Polyomaviruses, In: Knipe, D.M., Howley, P.M. (Eds.),
Fifth ed. Fields Virology, Vol. 2. Lippincott Williams and Wilkins, Philadelphia, PA, pp. 2263–2298.

Karalic, D., Lazarevic, I., Cupic, M., Jevtovic, D.J. and Jovanovic, T. (2014). Prevalence of JC and BK Polyomavirus Excretion in the Urine of HIV-Infected Patients from Serbia. Archives of Biology and Science 66 (2): 609-614.

Knowles, W.A., Pillay, D., Johnson, M.A., Hand, J.F. and Brown, D.W. (1999). Prevalence of long-term BK and JC excretion in HIV-infected adults and lack of correlation with serological markers. Journal of Medical Virology 59: 474–479.

Kruzel-Davila E., Sankofi B.M., Kubi Amos-Abanyie E., Ghansah A., Nyarko A., Agyemang S., Awandare G.A.,, Szwarcwort-Cohen M., Reiner-Benaim A., Hijazi B., Ulasi I., Raji Y.R., Boima V., Osafo C., May Adabayeri V., Matekole M., Olanrewaju T.O., Ajayi S., Mamven M., Antwi S., Ademola A.D., Plange-Rhule J., Arogundade F., Akyaw P.A., Winkler C.A., Salako B.L., Ojo A., Skorecki K., Adu D and the H3Africa Kidney Disease Research Network Investigators (2021). HIV Viremia Is Associated With APOL1 Variants and Reduced JC-Viruria. Front. Med. 8:718300. doi: 10.3389/fmed.2021.718300

Lafon, M., Dutronc, H., Dubois, V., Pellegrin, I., Barbeau, P., Ragnaud, J., Pellegrin, J. and Fleury, H.J.A. (1998). JC Virus Remains Latent in Peripheral Blood B Lymphocytes but Replicates Actively in Urine from AIDS Patients. The Journal of Infectious Diseases 177:1502–5.

Machado, D.M., Fink, M.C., Pannuti, C.S., Succi, R.C., Machado, A.A. and do Carmo, F.B. (2011). Human polyomaviruses JC and BK in the urine of Brazilian children and adolescents vertically infected by HIV. Mem Inst Oswaldo Cruz106:931-5.

Mubanga, E., Patel, A., Siddiqi, O. K., Hanson, B. A., Dang, X., Lakhi, S., Mulundu, G., Bender, N., & Koralnik, I. J. (2019). Progressive multifocal leukoencephalopathy in Zambia is caused by JC virus with prototype regulatory region. Journal of neurovirology, 25(4), 475–479. https://doi.org/10.1007/s13365-019-00746-x

Nali, L.H.S., Centrone, C.C., Urbano, P.R.P.,Penalva-De-Oliveira, A.C., Vidal, J.E., Miranda, E.P., Pannuti, C.S. and Fink, M.C.D. (2012). High Prevalence of the Simultaneous Excretion of Polyomaviruses JC and BK in the Urine of HIV-Infected Patients without Neurological Symptoms in São Paulo, Brazil. Revista do Instituto de Medicina de Tropical de Sao Paulo 54(4):201-205.

Nqebelele, N. U., Dickens, C., Dix-Peek, T., Duarte, R., & Naicker, S. (2019). JC Virus and APOL1 Risk Alleles in Black South Africans With Hypertension-Attributed CKD. Kidney international reports, 4(7), 939–945. https://doi.org/10.1016/j.ekir.2019.05.006.

Samah, A.L., Lamiaa, H., EL-Chaimaa, B.M., Salem, E.S.M., Emad, M.A., Entsar, E.A. and Amira, H.S. (2014). Detection of Human JC Polyomavirus DNA in Patients with Solid Tumors by Semi-Nested Polymerase Chain Reaction. Life Science Journal 11 (12): 918-927

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