THE ANGIOGRAPHIC APPEARANCE OF INTRACRANIAL ANEURYSMS IN HUMAN IMMUNODEFICIENCY VIRUS-INFECTED PATIENTS AT CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL

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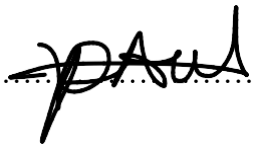
DECLARATION

I declare that this dissertation, which is submitted in consideration of the award of a Master of Medicine degree in Neurosurgery at the University of the Witwatersrand, is my own personal effort. Where any of the content presented is the result of input or data from a related collaborative research program, this is duly acknowledged in the text, such that it is possible to determine how much of the work is my own. I confirm that this work has not previously been submitted by me for a degree at this or any other university. Furthermore, I took sensible care to ensure that the work is original and, to the best of my knowledge, does not breach copyright law, and has not been taken from other sources except where such work has been cited and duly acknowledged within the text.

Initial & Surname :Saul-Macala…… Signature:  ……

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DEDICATION

I would like to dedicate this work to God, who has sustained me in this Journey. To my Family that has been very supportive, their words of encouragement, prayers during the entire training period from My Husband (Akhona Macala), my children (Anie, Mandla, Mihle), My Mother (Kosie), my sisters (Zan, Bee, Sekho), my Nephew (Ma-kk), my late grandmother (Nokondla), whose wise words are always a source of strength. To my friends, for the encouragement and support.

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List of Abbreviations

Acquired Immunodeficiency Syndrome ..... **AIDS**

Charlotte Maxeke Johannesburg Academic Hospital ..... **CMJAH**

Cluster of Differentiation 4 ..... **CD4**

Computed Tomographic Angiography ..... **CTA**

Digital Subtraction Angiography ..... **DSA**

Highly Active Antiretroviral Therapy ..... **HAART**

Human Immunodeficiency Virus ..... **HIV**

Human Research Ethics Committee ..... **HREC**

Interquartile Range ..... **IQR**

Millimeters ..... **mm**

National Health Laboratory Service ..... **NHLS**

People Living with HIV ..... **PLWH**

Picture Archiving and Communication System ..... **PACS**

Standard Deviation ..... **SD**

Statistical Package for the Social Sciences ..... **SPSS**

Subarachnoid Hemorrhage ..... **SAH**

Abstract

Background

Intracranial aneurysms can cause subarachnoid hemorrhage, which has a high risk of death and serious complications. HIV infection is known to cause problems in blood vessels, including the formation of aneurysms, mainly due to ongoing inflammation and damage to the inner lining of blood vessels (endothelial dysfunction). Although aneurysms related to HIV have been reported in children, there is not much information about adults, especially in places like South Africa, where HIV is very common. It is still unclear how a weakened immune system (measured by CD4 count) or treatment with highly active antiretroviral therapy (HAART) affects the shape and growth of these aneurysms. This study helps to fill that gap by looking at the angiographic features of intracranial aneurysms in people with and without HIV.

Aim of the study

To investigate the angiographic features of intracranial aneurysms in HIV-infected individuals and compare them with HIV-negative patients, while exploring associations with CD4 count and HAART status.

Methodology

We conducted a retrospective review by including 137 patients diagnosed with intracranial aneurysms at Charlotte Maxeke Johannesburg Academic Hospital from June 2014 to June 2022. Angiographic data from CTA and DSA were analyzed to assess aneurysm size, shape, and location. Patient records provided HIV status, CD4 count, and HAART therapy information. Aneurysm characteristics were compared between HIV-positive and HIV-negative groups, and statistical tests were used to evaluate associations with CD4 counts and HAART status.

Results

Among the 137 patients, 36 were HIV-positive and 26 were HIV-negative. No significant differences in aneurysm location or shape were found between the groups. However, a weak but significant negative correlation was observed between CD4 count and aneurysm height ($r = -0.348$, $p = 0.037$) and aspect ratio ($r = -0.440$, $p = 0.007$), indicating that lower CD4 counts were associated with larger aneurysms. HIV-positive patients on HAART had significantly larger aneurysm dimensions than those not on HAART (neck width $p = 0.035$, dome width $p = 0.013$, height $p = 0.006$), although aspect ratio did not differ significantly. Aneurysm rupture rates and the number of multiple aneurysms did not significantly differ between groups.

Conclusion

HIV status alone did not significantly alter aneurysm morphology or location; however, advanced immunosuppression (low CD4 count) and HAART therapy were associated with increased aneurysm dimensions. Immune status and antiretroviral treatment may influence aneurysm progression. Routine vascular screening may be warranted for immunosuppressed PLWH, especially those with additional vascular risk factors.

1. Introduction:

Patients with intracranial aneurysms often face hemorrhagic strokes. The rupture of an aneurysm usually results in subarachnoid hemorrhage, which results in high death rates, severe neurological problems, and long-lasting disability [1]. The prevalence of unruptured brain aneurysms is estimated to be about 1% to 3%, according to a recent study [2], while hypertension, smoking, and genetic factors are established risk factors for intracranial aneurysms [3, 4].

HIV infection leads to different types of vascular conditions that emerge because of chronic inflammation and endothelial dysfunction. These conditions include aneurysm formation together with accelerated atherosclerosis and vasculitis manifestations [5]. Research shows HIV-related fusiform aneurysms have been clinically identified among pediatric patients [6], yet similar evidence about adult patients is missing. There is limited knowledge about how immunosuppression affects artery physiology and anatomical structure, as measured by CD4 counts, and the aneurysmal development and structure both before and after highly active antiretroviral therapy (HAART) initiation. The literature shortage reveals minimal information about how HIV-positive patients, also known as people living with HIV (PLWH), exhibit intracranial aneurysms as well as their angiographic features. Therefore, this research investigates aneurysmal angiographic patterns presenting at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) among both PLWH and HIV-negative patients.

Both intracranial aneurysms and HIV infection are common conditions in our setting. Inevitably there will be patients who fall into both categories and given its known association with vasculopathy, it is to be expected that HIV co-infection will affect the phenotype of intracranial aneurysms in at least some of these patients. This may alter the clinical course of these patients in a multitude of ways and is a problem that is deserving of being studied further.

2. Literature Review:

2.1. Demographics:

Intracranial aneurysms are major cerebrovascular pathologies that possess a significant risk of rupture which leads to subarachnoid hemorrhage (SAH) with high morbidity rates and fatal outcomes, as well as non-rupture effects such as mass effect and thromboembolic phenomena. Global statistics show that unruptured intracranial aneurysms exist in about 2.8% of patients, while their yearly rupture risks range from 0.3% to 1.5% based on aneurysm dimensions and form together with individual health factors [7, 8]. There is research out there but

not in our setting (South Africa) regarding the prevalence and clinical results together with aneurysm features in PLWH who have intracranial aneurysms.

2.2. Risk Factors:

Intracranial aneurysm form when these risk factors exist:
Hypertension leads to damage of endothelial cells, which initiates aneurysm development [9]. Tobacco exposure through smoking leads to higher likelihood of aneurysm formation and rupture through its inflammatory process coupled with oxidative damage [10]. Different genetic conditions including autosomal dominant polycystic kidney disease and Ehlers-Danlos syndrome increase the chances of developing aneurysms. The risk for developing an aneurysm increases with age beyond 40 as well as among female patients [11].
The formation of aneurysms might cause either no symptoms or gradual growth that ends with arterial rupture and bleeding. The rupture of aneurysms most often leads to serious haemorrhagic conditions like SAH, which can result in approximately 30% of cases succumbing to the event and about 50% suffering severe disabilities [12].

2.3. HIV-Associated Cerebrovascular Disease:

HIV can cause vascular pathology through multiple mechanisms, such as chronic inflammation, endothelial dysfunction, and immune-mediated vascular injury [13]. HIV-associated vasculopathy includes Aneurysmal vasculopathy, characterized by fusiform, ectatic, or saccular aneurysms. HIV-related vasculitis does not occur in the absence of opportunistic infections [14], and result from inflammatory changes in the arterial wall triggered by such infections through viral or immune-mediated mechanisms [15]. Accelerated atherosclerosis in HIV patients leads to a higher prevalence of cardiovascular disease that causes aneurysm formation [5].

2.4. Aneurysm Prevalence and Morphology in HIV-Positive Patients:

A retrospective investigation performed in South Africa by Blignaut et al. demonstrated 41 aneurysms found within 23 PLWH. Most of the analyzed aneurysms appeared as saccular structures which formed in the anterior communicating artery and internal carotid artery. The analyzed aneurysm sac measurement averaged 5.0 millimeters, and broad-necked aneurysms predominated among the cases studied [16].

Three PLWH from South Africa received medical attention for intracranial aneurysms, according to Modi et al. The researchers of this series detected primarily fusiform aneurysms and CD4 cell counts varying from 4 to 970 cells/ml, unlike previous studies [17].

The research conducted by Law-Ye et al. involved five adult patients diagnosed with HIV who had fusiform aneurysms yet no hemorrhages. The patients remained stable with their aneurysms according to the researchers after starting antiretroviral therapy [18].

2.5. The Role of Immunosuppression in Aneurysm Development:

A strong association exists between low CD4 cell numbers and specific features of aneurysms. Medical researchers suggest that immune system conditions affect both aneurysm size and morphology, together with location features. One study found that PLWH with decreased CD4 counts presented both bigger aneurysms along with more complex aneurysmal shapes because of endothelial cell dysfunction [19]. Research by Thawani et al. showed that immune deficiency stands as the primary factor in the development of aneurysmal vasculopathy among PLWH instead of viral pathogenesis directly causing this issue [20].

Medical researchers conducting intracranial aneurysm studies on both PLWH and HIV-negative patients have generated inconsistent results. Such as a study by Juchler et al., showed that aneurysm shape remains equivalent between HIV-infected patients and those who are not PLWH [21]. Another study found that PLWH might develop fusiform aneurysms with broad necks, mainly in the anterior part of the brain [22]. Thus, studies remain inconclusive about whether PLWH develop multiple aneurysms compared to patients without HIV.

2.6. Effect of HAART on Intracranial Aneurysms:

HAART substantially boosts survival expectancy for PLWH yet the medications' effects on vascular health remain unclear [23]. Research shows two conflicting effects of HAART therapy on vascular inflammation where the treatment might stabilize aneurysms yet protease inhibitors may trigger endothelial dysfunction and atherosclerosis [24]. A recent study found that PLWH under anti-retro viral therapy had bigger aneurysms than non-treated patients because extended life expectancy allowed additional vascular damage to accumulate [5]. According to Hoz et al., rupture rates of aneurysms remained similar between patients on HAART medications and those without HAART treatment. This data implies that HAART does not affect stability patterns of aneurysms directly [25].

2.7. Gaps in Literature and Need for Further Research:

Current research has various limitations due to small sample sizes, insufficient studies on control groups, and a lack of long-term outcome data. Most research on PLWH involved small sample groups below 50 participants. Some research studies fail to examine relationships between both PLWH and HIV-negative patient groups through direct comparison. Some lack tracking of HIV-related aneurysm development into the future. Because South Africa has high HIV rates, with prevalence among women rising from 22% in 2002 to 29% by 2017, and nearly 46% unaware of their HIV risk [26], it becomes crucial to conduct additional studies which detail the relationship between HIV infections along with immunodeficiency and aneurysm manifestations.

3. Research Question:

Does HIV infection predispose patients to a distinct pattern of intracranial aneurysm characteristics compared to the general population, and does immunosuppression (as measured by CD4 count) or HAART therapy influence these characteristics?

4. Hypothesis:

PLWH will have aneurysms that differ in site, size and morphology from those found in HIV negative patients, and that the degree of immunosuppression as measured by CD4 count and/or taking of HAART medication will affect these findings.

5. Aims and Objectives:

The aim is to undertake a comprehensive angiographic analysis of intracranial aneurysms in PLWH and HIV-negative patients, in order to establish the effect of HIV infection, CD4 count and HAART therapy on aneurysms characteristics.

Objectives are as follows:

1. Describe the demographic characteristics of patients presenting with intracranial aneurysms.

2. Compare the angiographic characteristics (location, morphology, size) of aneurysms between PLWH and HIV-negative individuals.
3. Investigate the correlation between CD4 count and aneurysm characteristics.
4. Assess whether HAART therapy influences aneurysm morphology and size.

5. Research Methodology:

5.1. Study Design

The researcher designed this retrospective study based on data obtained at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH). Hospital records provided research data from June 2014 to June 2022, an eight-year period.

5.2. Study Site

The research took place at CMJAH. It is a tertiary care hospital situated in Johannesburg, South Africa. As a major referral center, CMJAH is equipped to provide specialized neurosurgical care to patients referred from surrounding healthcare facilities. CMJAH maintains neuroimaging equipment such as Computed Tomographic Angiography (CTA) and Digital Subtraction Angiography (DSA) for regular intracranial aneurysm diagnosis purposes. This study relied on the hospital's electronic medical records, laboratory databases, and the Picture Archiving and Communication System (PACS) to retrieve relevant clinical and radiological data.

5.3. Study Population

The patients diagnosed with intracranial aneurysms at CMJAH from June 2014 to June 2022 were included in the study.

5.4. Inclusion Criteria:

All patients diagnosed with intracranial aneurysms during the study period were included in the study.

5.5. Exclusion Criteria:

Patients with missing patient records. Patients with either traumatic aneurysms or mycotic aneurysms or known congenital vascular malformations were excluded from the study.

5.6. Sample size:

During the study period, a total of 162 patients with diagnosed intracranial aneurysms were initially identified. Of these, 25 were excluded due to missing or incomplete imaging data, resulting in a final sample size of 137 patients. Among the included patients, 84 had ruptured aneurysms and 53 had unruptured aneurysms. A study flow diagram illustrates patient selection and final sample size (Figure 1).

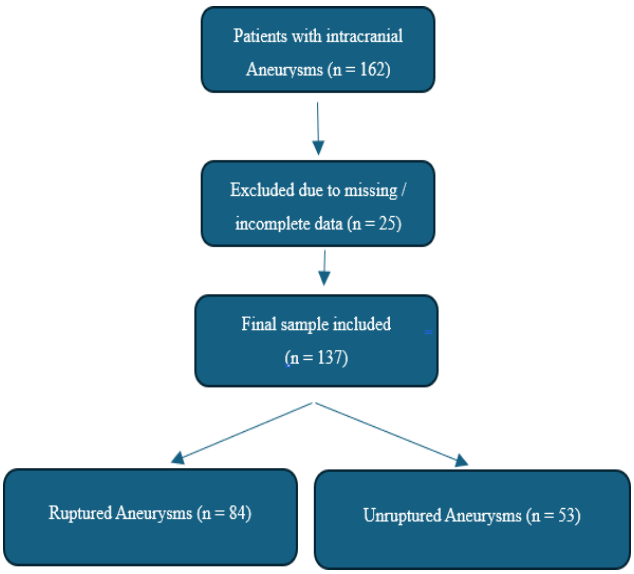

Figure 1. Flow diagram showing patient selection and sample size.

5.7. Data Collection Tool/Instrument:

CTA and DSA images stored in the PACS system were used by the observers to obtain all measurements of intracranial aneurysms, including size, location, and morphological features. Two observers conducted independent reviews of the measurements recorded in millimeters. The primary investigator worked with a supervising radiologist to perform these reviews. When observers obtained different measurements, the case was sent to a senior neuroradiologist for a final reading.

Information regarding CD4 counts was sourced from National Health Laboratory Service (NHLS) that operates a nationwide archive of laboratory test results within South African public medical facilities. Patient

data regarding HAART therapy status came from clinical file reviews which contained records of treatment regimens and their start dates.

5.8. Data Collection Process:

Data extraction took place from both electronic hospital records as well as from the PACS imaging database. Demographic characteristics were documented for each patient, including age, gender, and race information. HIV-related data came from laboratory and clinical records where medical staff obtained serostatus results together with CD4 count minimum values and treatment status under HAART therapy.

Healthcare professionals systematically examined aneurysm properties by using data from both CTA and DSA evaluations. Each documented aneurysm received classification based on its position between anterior or posterior circulation types by measuring its specific location through anterior communicating artery, middle cerebral artery, internal carotid artery or basilar artery and posterior cerebral artery. The number of aneurysms was also counted to determine if each patient had one or several aneurysms. Aneurysms were further classified into saccular, fusiform, lobulated, bilobed, and trilobed patterns for assessment. A study of aneurysm geometric properties was conducted by measuring the size parameters that consisted of neck width and dome width as well as height and aspect ratio.

5.9. Bias Mitigation:

Multiple strategies were implemented to eliminate bias both during data recording and during the research analysis phase. The researchers established uniform criteria to select patients that ensured consistent patient selection. Two independent readers conducted imaging evaluations to reduce measurement errors which a senior neuroradiologist decided if their conclusions differed. Hospital official records together with NHLS laboratory data were utilized to minimize information bias because both systems provide standardized documentation for HIV-related parameters.

6. Ethics:

This research gained approval through the University of the Witwatersrand Human Research Ethics Committee (HREC) to fulfill the necessary ethical standards for research. The CMJAH administration granted researchers access to clinical records for collecting data through their permission.

Patient records were de-identified before data collection when each case received a specific study code that preserved patient confidentiality. The research team was the only group able to access data stored on a password-protected computer where data was safely kept. Since both patient contact and interventions were excluded from the retrospective study design, the ethics committee granted an exemption from the need to obtain informed consent.

7. Data Analysis

Data were entered into an Excel spreadsheet and then exported to IBM SPSS version 27 for statistical analysis. Descriptive statistics were used to summarize patient demographics and aneurysm characteristics. Categorical variables, such as gender and aneurysm location, were expressed as frequencies and percentages. Continuous variables, including aneurysm size measurements, were summarized using means and standard deviations for normally distributed data, while medians and interquartile ranges were used for non-normally distributed data. Comparative statistical tests were applied to assess differences between PLWH and HIV-negative groups. Chi-square and Fisher's exact tests were used to analyze categorical variables. Independent t-tests were conducted for normally distributed continuous variables, while the Mann-Whitney U test was applied to non-normally distributed continuous variables. To explore the relationship between CD4 count and aneurysm dimensions, Spearman's correlation coefficient was calculated. A p-value of less than 0.05 was considered statistically significant.

8. Results:

8.1. Demographics:

A total of 137 patients with intracranial aneurysms were included in the study. The majority were female (n = 89, 65.0%), while 48 (35.0%) were male. The mean age of participants was 47.4 ± 13.52 years. The most prevalent age group was 51-60 years (n = 41, 29.9%), followed by 41-50 years (n = 37, 27.0%) as shown in Figure 1. The majority of patients were Black (n = 110, 80.3%), while 24 (17.5%) were White, 2 (1.5%) were Colored, and 1 (0.7%) was Indian, as shown in Table 1 & Figure 2.

Table 1. Sociodemographic characteristics of study participants (n=137).

	n	%
Gender		
Female	89	65.0%
Male	48	35.0%
Age groups (years)		
11-20	3	2.2%
21-30	13	9.5%
31-40	21	15.3%
41-50	37	27.0%
51-60	41	29.9%
> 60	22	16.1%
Age (years), mean ± SD	47.4 ± 13.52	
Race		
Black	110	80.3%
Colored	2	1.5%
Indian	1	0.7%
White	24	17.5%

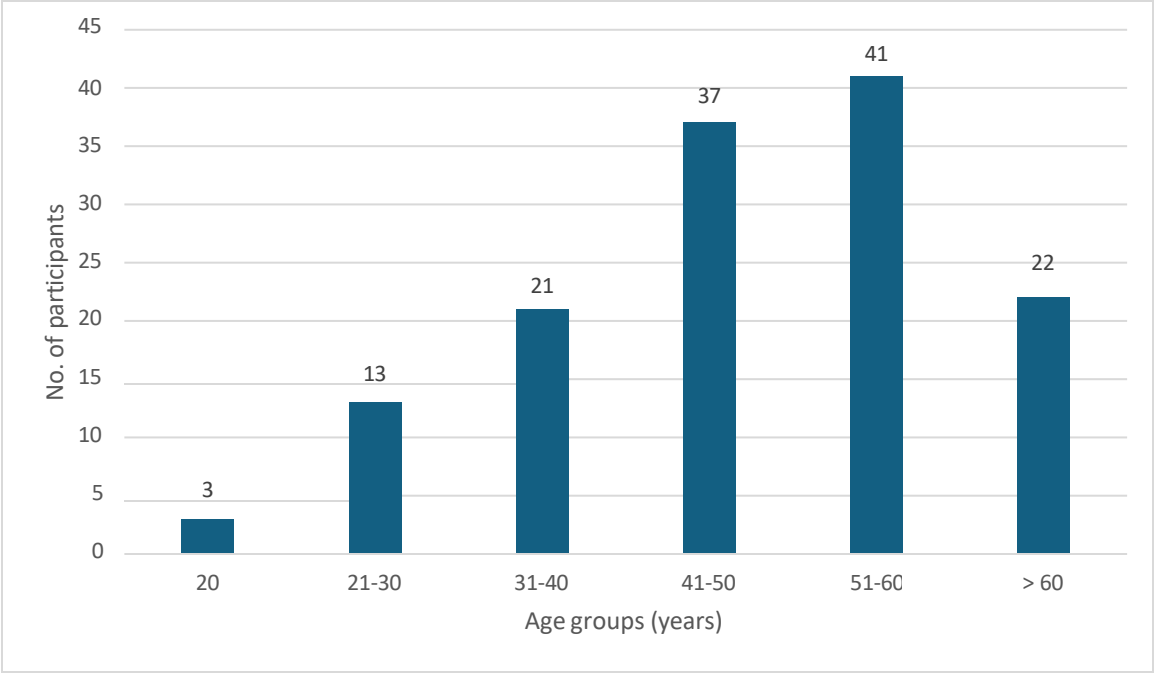

Figure 2. Distribution of patients based on age groups.

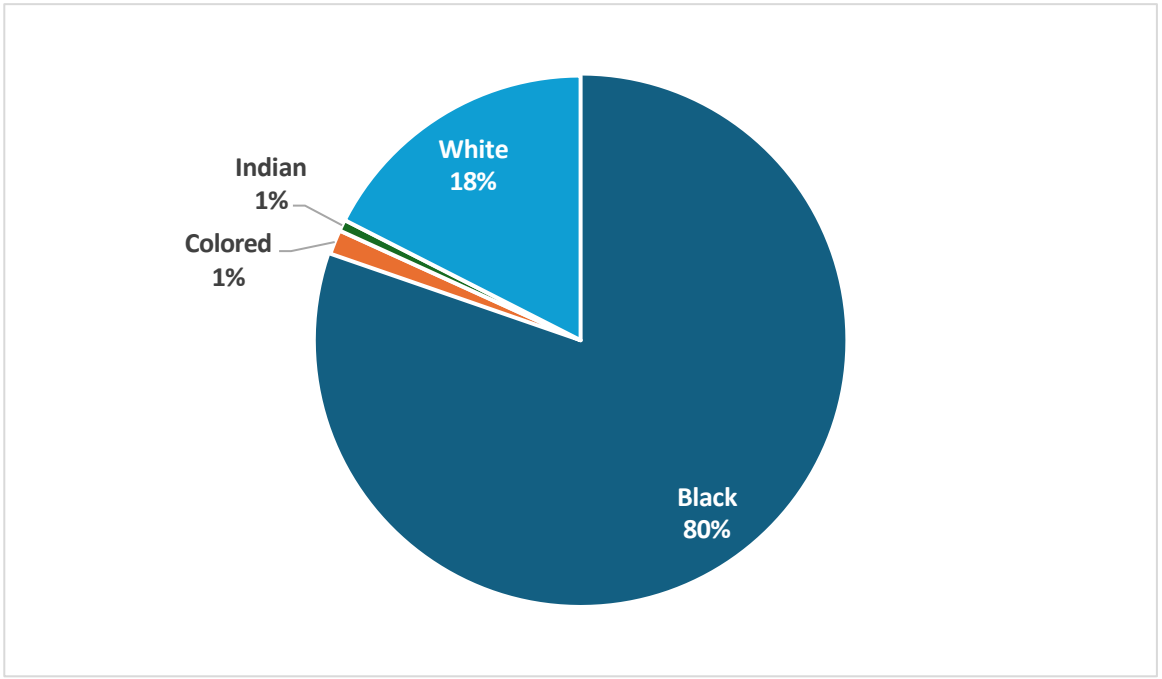

Figure 3. Pie chart depicting the number of participants of each race.

8.2. Distributions and Shapes of Aneurysms:

Aneurysms were more commonly located in the anterior circulation, with the anterior communicating artery being the most frequently affected site (n = 47 out of 130 anterior circulation aneurysms, 36.2%), as shown in Figure 3. Posterior circulation aneurysms were rare, with the basilar artery being the most affected (n = 3 out of 7 posterior circulation aneurysms, 42.9%), as shown in Figure 4. The majority of aneurysms were saccular (n = 124 out of 137 total aneurysms, 90.5%), followed by fusiform (n = 6, 4.4%), lobulated saccular (n = 4, 2.9%), bilobed saccular (n = 2, 1.5%), and trilobed saccular (n = 1, 0.7%) as shown in Table 2.

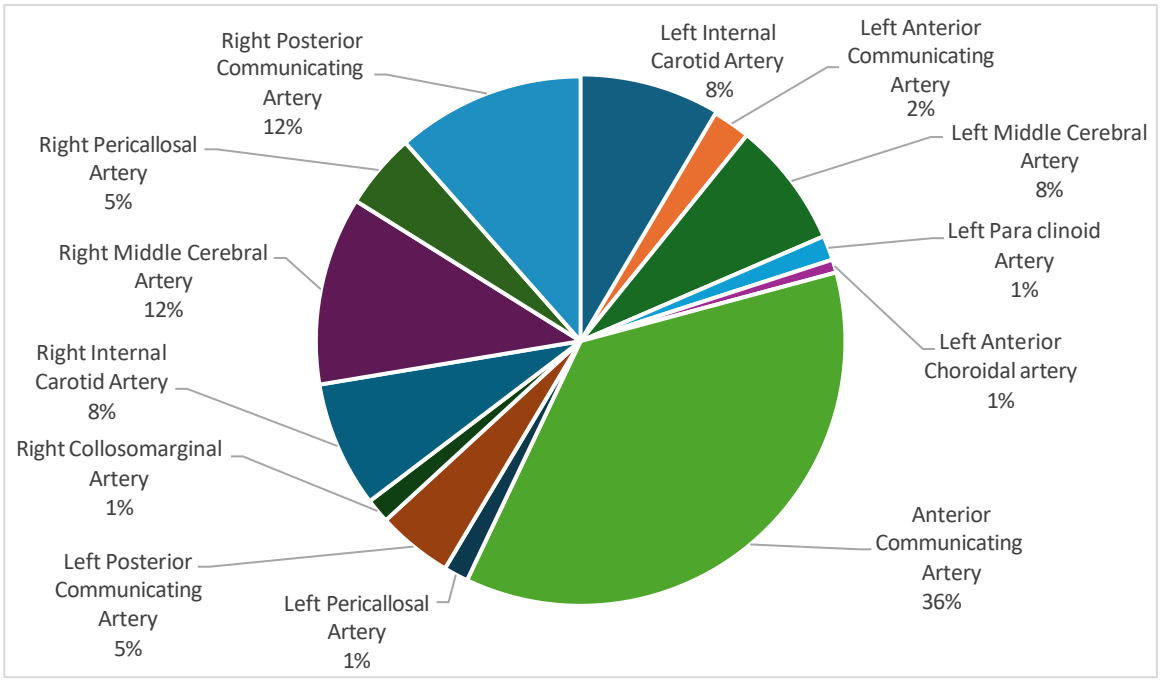

Figure 4. Pie chart representing the distribution of anterior circulatory aneurysms.

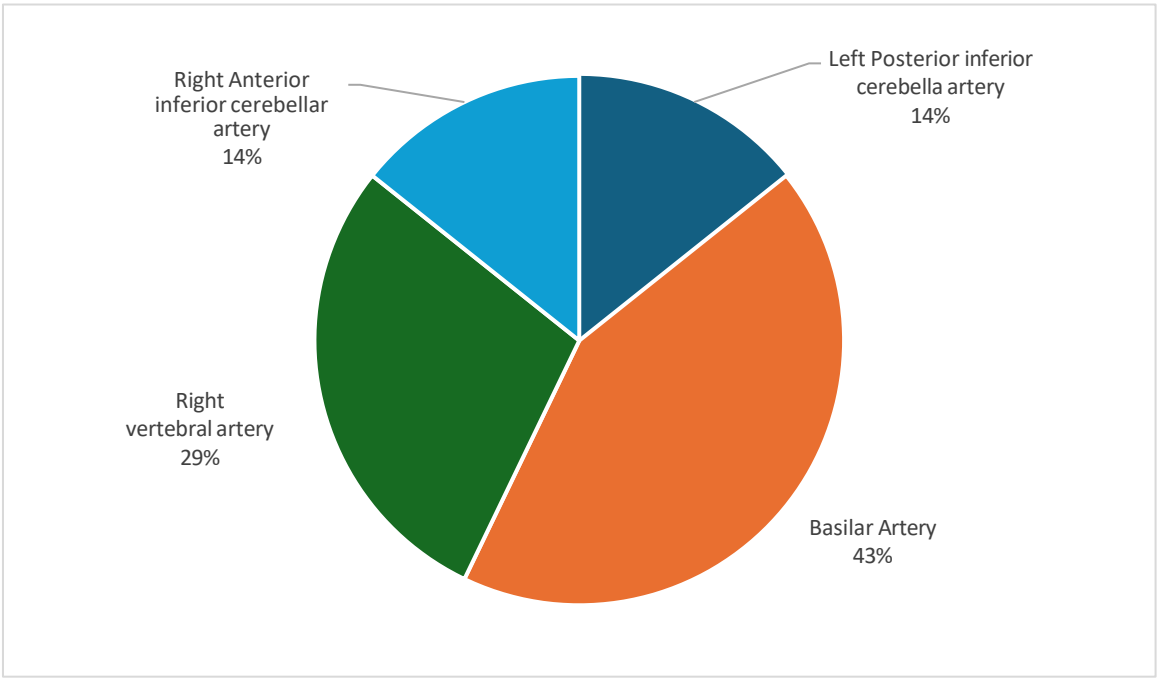

Figure 5. Pie chart representing the distribution of posterior circulatory aneurysms.

Table 2. Different shapes of aneurysm.

Shape of Aneurysm	n	%
Bilobed saccular	2	1.5%
Fusiform	6	4.4%
Lobulated saccular	4	2.9%

Saccular	124	90.5%
Trilobed saccular	1	0.7%

8.3. Dimensions, diagnosis, andnumbers of Aneurysms:

The median neck width of aneurysms was 3.20 mm (IQR: 2.00 - 4.99 mm), the median dome width was 5.17 mm (IQR: 3.20 - 7.68 mm), and the median height was 5.10 mm (IQR: 3.10 - 8.00 mm). The median aspect ratio (defined as the height of the aneurysm divided by its neck width) was 1.50 (IQR: 1.12 - 2.25 mm), as shown in Table 3. Multiple aneurysms were present in a small proportion of patients, with 7 (5.1%) having one extra aneurysm and 4 (2.9%) having two extra aneurysms (Table 4). Most aneurysms were identified using both CTA and DSA (n = 104, 75.9%), while 33 (24.1%) were detected using CTA alone (Table 5).

Table 3. Different dimensions of aneurysm.

Aneurysm dimensions	Median (mm)	IQR (mm)
Neck width	3.20	2.00 - 4.99
Dome width	5.17	3.20 - 7.68
Height	5.10	3.10 - 8.00
Aspect Ratio	1.50	1.12 - 2.25

Table 4. Presence of multiple aneurysm (more than one) in patients.

	n	%
1 extra aneurysm	7	5.1%
2 extra aneurysms	4	2.9%

Table 5. Imaging modality used to identify aneurysms.

Imaging methods	n	%
CTA and DSA	104	75.9%
CTA	33	24.1%

CTA: Computed Tomographic Angiography; DSA: Digital Subtraction Angiography.

8.4. Characteristics of Aneurysms:

Among the study participants, 36 were PLWH and 26 were HIV-negative, while remaining participants (n = 75) have unknown status for HIV. Aneurysm location was similar between groups, with anterior circulation aneurysms being the most prevalent in both PLWH (n = 33, 91.7%) and HIV-negative patients (n = 25, 96.2%; p = 0.633). The shape of aneurysms also showed no statistically significant difference between groups (p = 0.241). The median aneurysm dimensions, including neck width, dome width, height, and aspect ratio, were comparable between PLWH and HIV-negative patients, with no significant differences observed (p > 0.05 for all comparisons), as shown in Table 6.

Table 6. Comparison of angiographic characteristics of aneurysm between HIV -positive and HIV -negative patients.

	HIV Status		p value
	Positive (n=36)	Negative (n=26)	
Location of Aneurysm, n (%)			
Anterior	33 (91.7%)	25 (96.2%)	0.633[a]
Posterior	3 (8.3%)	1 (3.8%)	
Shape of Aneurysm, n (%)			
Bilobed saccular	1 (2.8%)	0 (0.0%)	
Fusiform	5 (13.9%)	1 (3.8%)	0.241[a]
Lobulated saccular	2 (5.6%)	0 (0.0%)	
Saccular	28 (77.8%)	25 (96.2%)	
Aneurysm dimensions, median (IQR)			
Neck width	3.64 (2.17 - 4.85)	3.15 (1.30 - 5.00)	0.628[b]
Dome width	4.36 (3.31 - 6.96)	5.34 (3.80 - 7.80)	0.343[b]
Height	5.49 (3.69 - 8.38)	4.20 (2.60 - 8.33)	0.304[b]
Aspect Ratio	1.48 (1.17 - 2.25)	1.60 (1.04 - 2.00)	0.549[b]

[a] Fisher exact test; [b] Mann-Whitney U test.

8.5. Correlation between CD4 count and aneurysm dimensions:

A weak negative correlation was found between CD4 count and aneurysm height (r = -0.348, p = 0.037) and aspect ratio (r = -0.440, p = 0.007), indicating that lower CD4 counts were associated with larger aneurysm heights and higher aspect ratios. No significant correlation was observed between CD4 count and neck width (r = -0.039, p = 0.819) or dome width (r = -0.235, p = 0.169) as shown in Table 7.

Table 7. Correlation between CD4 count and aneurysm dimensions.

Aneurysm dimensions	CD4 Count	
	Correlation Coefficient (r)	p value
Neck width	-0.039	0.819
Dome width	-0.235	0.169
Height	-0.348	0.037
Aspect Ratio	-0.440	0.007

8.6. Aneurysms between HAART and Non-HAART group:

Among PLWH, 19 had initiated HAART, while 17 had not. The location of aneurysms did not significantly differ between these groups (p = 1.000). The shape of aneurysms also showed no significant variation (p = 0.168). However, aneurysm dimensions were significantly larger in the HAART-initiated group compared to the non-initiated group. Median neck width was greater in HAART users (3.82 cm, IQR: 3.00 - 5.55 cm) compared to non-users (2.76 cm, IQR: 1.59 - 3.90 cm; p = 0.035). Similarly, dome width (p = 0.013) and height (p = 0.006) were significantly larger in HAART users. Aspect ratio did not differ significantly between the two groups (p = 0.707) as shown in Table 8.

Table 8. Comparison of angiographic characteristics of aneurysm between HAART initiated group and non-HAART initiated group.

	HAART Initiated		p value
	Yes (n=19)	No (n=17)	
Location of Aneurysm, n (%)			
Anterior	17 (89.5%)	16 (94.1%)	1.000[a]
Posterior	2 (10.5%)	1 (5.9%)	
Shape of Aneurysm, n (%)			
Bilobed saccular	0 (0.0%)	1 (5.9%)	
Fusiform	4 (21.1%)	1 (5.9%)	0.168[a]
Lobulated saccular	2 (10.5%)	0 (0.0%)	
Saccular	13 (68.4%)	15 (88.2%)	
Aneurysm dimensions, median (IQR)			
Neck width	3.82 (3.00 - 5.55)	2.76 (1.59 - 3.90)	0.035[b]
Dome width	5.65 (4.00 - 7.74)	3.70 (2.76 - 4.67)	0.013[b]
Height	6.80 (4.60 - 10.80)	4.30 (2.47 - 5.60)	0.006[b]

Aspect Ratio	1.50 (1.11 - 2.61)	1.46 (1.19 - 1.94)	0.707[b]

[a] Fisher exact test; [b] Mann-Whitney U test.

9. Discussion of results/findings:

9.1. Demographics andoverview:

This study presents angiographic properties of intracranial aneurysms in PLWH, along with a comparison of relevant aneurysm characteristics between PLWH and HIV-negative patients. This study evaluated 137 patients carrying intracranial aneurysms, where 36 among them are PLWH, and found little difference regarding aneurysm location, morphology and size between patients who were HIV positive and negative. Patients with lower CD4 counts demonstrated increased dimensions in their aneurysm measurements, especially height and aspect ratio values. Subjects on HAART showed increased aneurysm dimensions as an outcome compared to treatment-naive patients.

9.2. Distributionand shape of aneurysms:

Intracranial aneurysms frequently occur in the anterior circulation, and the anterior communicating artery represents the region with maximum incidence according to this study's findings. The anterior circulation occupies 80-90% of all intracranial aneurysms, according to research involving the general population [27]. Haemodynamic stress affects the anterior communicating artery aneurysms the most, according to a recent study [28], which explains their frequent appearance in both PLWH and HIV-negative patients in our study patients. The distribution among both groups with and without HIV remains similar since HIV infection shows no substantial effect on aneurysm location in the brain.

The majority of aneurysms were classified as saccular, while fusiform and lobulated aneurysm types were less prevalent. Other studies show that saccular aneurysms exist at the highest levels in both PLWH and HIV-negative population groups. The study by Bruno et al. detected a greater number of fusiform aneurysms in PLWH [6]. The differences in sample sizes and imaging technologies together with patient selection variations probably explain this result discrepancy. Patients who maintained lower CD4 cell counts showed a tendency towards increased aneurysm size complexity, although statistics did not demonstrate a distinct shape difference between those with or without HIV infection.

9.3. Correlationbetween CD4 count andaneurysm dimensions:

One of the main findings showed that CD4 count negatively related to aneurysm height ($r = -0.348$, $p = 0.037$) and aspect ratio ($r = -0.440$, $p = 0.007$). The patients with more advanced stages of HIV develop bigger aneurysms that feature longer heights when compared to their neck diameter. According to White et al. (2023), lower CD4 counting among PLWH resulted in the development of larger aneurysms [29]. The aneurysm development is linked to HIV-caused endothelial dysfunction alongside chronic inflammation and vasculitis that harm vascular walls and advance aneurysm growth [24].

9.4. Aneurysms between HAART and Non-HAART group:

Our study also found that individuals under HAART therapy exhibited significantly enlarged aneurysms compared to patients without HAART therapy. Other researchers found that neck width along with dome width and height became larger across the HAART-treated population. It noted that extended survival because of HAART therapy permitted aneurysm growth throughout time [30]. Research on the artery modifications brought by HAART presents conflicting results. Research points to both positive and negative findings about antiretroviral therapy since it may decrease inflammation while protecting vascular health, but certain protease inhibitors might trigger artery narrowing and blood vessel problems [30, 31]. Additional research is required because scientists need to understand the complete vascular impacts of HIV medication therapy administered for extended periods to PLWH.

9.5. Correlation of Aneurysm rupture and HIV status:

The study findings did not show a significant difference in aneurysm rupture rates between individuals with and without HIV, as aneurysm dimensions were influenced by CD4 count levels and HIV treatment status. The results differed from other researches, which showed that fusiform aneurysms linked to HIV had a low potential for rupture even though they were relatively large [6]. The study results demonstrated no significant variations in rupture rates which implies aneurysm size variation might be affected by immune status but other factors like haemodynamic stress and arterial wall composition and genetic predisposition dominate aneurysm stability [32].

9.6. Number of aneurysms:

Many patients presented with single aneurysms because only 7 (5.1%) among them had one additional aneurysm while 4 (2.9%) had two extra aneurysms. The number of patients with multiple aneurysms remains lower than a prior study results which reported such cases in up to 20-25% of patients. The results showing fewer cases of multiple aneurysms in this study could be due to genetic factors and environmental conditions that control the pathophysiology of aneurysms in South African populations [33]. The study may demonstrate low detection rates of small aneurysms during the initial diagnostic imaging assessment process.

9.7. HIV status andaneurysm development:

The study findings contribute to scientific discussions regarding HIV-related brain aneurysm predisposition mechanisms since the research shows no direct link between aneurysm development and HIV status independent of co-occurring vascular risks. The similar locations and morphological characteristics of aneurysms in PLWH and HIV-negative patients implies that HIV presence alone fails to establish its role as the aneurysm development cause [19]. The HIV-related damage to blood vessels appears to increase the growth of aneurysms among specific individuals who also present low CD4 counts. Ongoing research must follow PLWH with reduced CD4 counts to establish if these patients form aneurysms at speeds that differ from those of HIV-negative patients.

9.8. Clinical Implications:

The study results yield essential clinical implications for healthcare practice. Healthcare providers need to establish screening protocols for blood vessel assessment in PLWH experiencing immunodeficiency symptoms specifically among those who also have hypertension or smoke. Studies should conduct further investigations to determine how different antiretroviral drug classes impact the development and risk of rupture in aneurysms.

10. Conclusion and Recommendations:

This study explored the angiographic characteristics of intracranial aneurysms in PLWH and how they compare with HIV-negative individuals. While no significant differences were observed in aneurysm location or morphology, lower CD4 counts were found to be associated with larger aneurysm height and higher aspect

ratios. Patients on HAART therapy had significantly larger aneurysm dimensions than those not receiving treatment, which shows the need for further research on the vascular effects of antiretroviral therapy. While HIV infection alone may not directly predispose individuals to aneurysm formation, advanced immunosuppression and long-term HAART therapy may influence aneurysm size and progression.

Given these findings, routine vascular screening should be considered for immunosuppressed PLWH, especially those with additional risk factors. Further prospective studies are needed to explore the long-term impact of HIV and antiretroviral therapy on cerebrovascular health.

11. Limitations:

This study contains some limitations. Its retrospective design depends on existing medical records while dealing with important data collection issues that affect both aneurysm size evaluation and HIV-related duration of HAART treatment. The research conducted at CMJAH within a single medical center limits the findings from being applied to populations with demographics and genetics beyond this community. A complete analysis of confounding variables including hypertension, smoking and additional cardiovascular conditions was not incorporated into the statistical analysis leading to possible effects on measured associations. Future research should adopt prospective multi-center designs with larger subject groups who undergo continued follow-up examinations to strengthen current findings.

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