

# A new look at human immunodeficiency virus infection and stroke in Sub-Saharan Africa

Engelbert Bain Luchuo<sup>1</sup>, Clovis Nkoke<sup>2</sup>

<sup>1</sup>Department of Military Health, Ministry of Defense, Yaounde, Cameroon; <sup>2</sup>Department of Internal Medicine and Specialties, Faculty of Medicine and Biomedical Sciences, University of Yaounde I, Yaounde, Cameroon

*Correspondence to:* Clovis Nkoke, MD. Department of Internal Medicine and Specialties, Faculty of Medicine and Biomedical Sciences, University of Yaounde I, Yaounde, Cameroon. Email: cnkoke@yahoo.com.

**Abstract:** Stroke and human immunodeficiency virus (HIV) infection are major causes of morbidity and mortality in Sub-Saharan Africa (SSA), with disease burdens being amongst the highest worldwide. HIV infection has emerged as an important risk factor for stroke. The remarkable development in the treatment of HIV infection which occurred in recent decades has allowed the survival of a large number of patients. This therapeutic success which allows patients to live longer has facilitated the emergence of a new population of adults with increased risk for cardiovascular disease including stroke due to aging, the direct effects of HIV infection and combined anti-retroviral therapy (cART). Preventive strategies to decrease the burden of stroke amongst this specific patient population remain understudied in this region of the world. Lack of early diagnosis (CT scans) and poor record keeping make appreciation of the burden difficult. There is indisputable evidence that early diagnosis and early placement on cART therapy reduce HIV associated morbidity and mortality in this region of the world. However, the emergence of a new population of patients at risk for developing stroke (HIV patients) who fortunately live longer deserves a keener attention. Long term effects of cART regimens on cardiovascular and metabolic profiles remain uncertain, and specific cohort studies to properly ascertain its consequences are needed. The evidence and specific guidelines with regards to anti-platelet therapies and statin use, though potentially beneficial, in this patient sub group remains scarce. African specific cohort studies including HIV positive patients in our opinion should constitute a top research priority, to properly ascertain the potential roles of anti-platelet therapies and statins with regards to primary and secondary prevention of stroke, as well as long term effects of cART on their cardiovascular and metabolic profiles.

**Keywords:** Human immunodeficiency virus (HIV); stroke; Sub-Saharan Africa (SSA)

Submitted May 19, 2016. Accepted for publication Jun 10, 2016.

doi: 10.21037/atm.2016.06.15

**View this article at:** <http://dx.doi.org/10.21037/atm.2016.06.15>

## Introduction

Stroke is the third leading cause of death and a leading cause of adult long-term neurological disability worldwide. The burden of stroke is however unevenly distributed with two thirds of all stroke deaths occurring in low and middle income countries including Sub-Saharan Africa (SSA) (1-3). Simultaneously, SSA bears the greatest burden of human immunodeficiency virus (HIV) infection worldwide. Not only is this a potential developmental challenge since the young and active population is the most affected, health system capacities in this region of the world to offer

adequate diagnostic, therapeutic and appropriate post stroke rehabilitation services have been surpassed (4). The advent of combined anti-retroviral therapy (cART) has enabled the prolongation of life of HIV infected patients. Infection with HIV has emerged as an important risk factor for stroke (5-7). This double burden of disease in the context of limited resources calls for urgent attention in reinforcing preventive measures that could reduce the incidence of stroke amongst these patients. The current view revisits key published knowledge on stroke in HIV infected patients in SSA and presents the place of key potential avenues for stroke

prevention in HIV infected patients.

Generally, patients with stroke in SSA are younger, compared to patients in western countries (5-7). In a study in Malawi, 67% of stroke patients with HIV infection were younger than 45 years (5). Heikinheimo and colleagues in Malawi have shown that, in addition to being younger, HIV infected patients with stroke have less traditional risk factors for stroke (8). This might suggest that the mechanism of HIV associated stroke may be independent of classical vascular risk factors.

Timely initiation of cART, and measures to improve compliance to therapy could indirectly reduce stroke morbidity and mortality that could arise from opportunistic infections (*Nocardia*, tuberculous meningitis, neurosyphilis) and central nervous system lymphomas.

### **Considering the role of low dose aspirin in patients with HIV infection for stroke prevention**

Patients who suffer from one or more cardiovascular events, such as myocardial infarction or ischemic stroke, are at very high risk for recurrent vascular events. Secondary prevention following a serious cardiovascular event is compelled by the high risk for a repeat event. However, initial cardiovascular events can be fatal or disabling, making primary prevention an important consideration as well (9). There is body of evidence that shows that aspirin is beneficial in the secondary prevention of vascular disease (10). But the benefit of aspirin in primary prevention has been conflicting. About 90 % of stroke amongst HIV infected persons are ischemic (5,6,8).

Low dose aspirin use sounds reasonable since about 90% of strokes amongst this sub group are ischemic in origin (5,6,8). Aspirin is widely available and very inexpensive and can reduce the risk of major cardiovascular events including stroke. There is substantial evidence that shows that low dose aspirin is beneficial in the secondary prevention of cardiovascular disease including stroke but the benefit is less certain for primary prevention (10). Research is ongoing with regards to other anti-platelet therapies or combinations with or without low dose aspirin. Low dose aspirin use still has its place and current state of art evidence and recommendations are sparse and mostly non-conclusive. This further emphasizes the essence of undertaking studies amongst persons living with HIV to be able to justify, in case of need, specific guidelines amongst this patient sub group. Though most stroke cases reported amongst HIV patients were ischemic (5,6,8), the inability to make an acute

diagnosis to distinguish ischemic from hemorrhagic stroke in acute stroke (scarcity and unaffordable CT scans) care could be a limiting factor to vulgarize low dose aspirin use in this context.

It might be interesting to develop risk assessment tools in patients with HIV infection since the disease has gradually shifted from an acute infection to a chronic one with an increased risk of cardiovascular events. This may help detect high risk patients who may need low dose aspirin. CT scanning machines are not only imperative in distinguishing ischemic from hemorrhagic strokes, critical for making acute care therapeutic decisions, but would be of utmost importance for appropriate differential diagnosis.

### **Statins and stroke**

It is known that HIV infection and cART could worsen cardiovascular and metabolic profiles amongst infected patients, making them more prone to adverse cardiovascular events including stroke (5-8). Statins are effective in reducing mortality and morbidity in patients with established cardiovascular disease including stroke, and also in people with higher levels of risk factors who have not yet developed clinically manifest CVD.

Two key questions remain unanswered: Whether being HIV positive alone is sufficient enough to deserve systematic placement on anti-platelet or statin therapy and whether specific guidelines for primary and secondary prevention of stroke are worth developing. The second question sounds more of an imperative considering the ever growing stroke incidence, mortality and morbidity in SSA (1-4).

### **Conclusions and future directions**

Current evidence suggests that HIV infection is an independent risk factor for stroke. In SSA where the burden of these two conditions is greatest, we have no doubt that the future may continue to be gloomy in case appropriate preventive and therapeutic measures are not put in place. Poor quality data, inaccessibility to diagnosis (CT scan) and unavailability of large population studies/evidence make ascertaining properly the burden and probable avenues for intervention difficult. Hypertension still remains a key risk factor for stroke in both HIV positive and negative persons. Early diagnosis and management must remain a key priority. Primary prevention must constitute the main approach to avert the continuous progression of cardiovascular risk and burden in Africa, which continues to demand remedial

strategies that are too costly, too limited, and often too late. Making CT scans more and more available and affordable cannot be overemphasized. It is unknown however if there are any preferences with regards to choice of antihypertensive drugs specific to persons living with HIV. Considering the risk of bleeding with anti-platelet therapies and other anticoagulants, as well as adverse reactions from statins and cART, a holistic clinical appraisal should remain the cornerstone of care, where choices of drug combinations with highest risk—benefit ratios should be prioritized. It is imperative to initiate large cohort studies in black African countries to ascertain the place of antiplatelet therapies (low dose aspirin) and statins amongst people living with HIV. This could also be an opportunity to properly ascertain the long term consequences of cART on the cardiovascular and metabolic risk profiles of persons living with HIV in Africa.

### Acknowledgements

None.

### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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**Cite this article as:** Luchuo EB, Nkoke C. A new look at human immunodeficiency virus infection and stroke in Sub-Saharan Africa. *Ann Transl Med* 2016;4(12):246. doi: 10.21037/atm.2016.06.15