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The study of association of stroke in human immunodeficiency virus infected patients

Vilas Honnakatti, Giridhar Patil
Assistant Professor, Department of General Medicine, Belagavi Institute of Medical Sciences & Hospital, Belagavi, Karnataka, India

Abstract
Introduction: Stroke in HIV is increasing in the developed countries from the data & studies. To say HIV infection as one of the risk factor for stroke is not known and the mechanism still being unclear. HIV is an emerging etiology for stroke in the young, particularly in a population with high seroprevalence for retroviruses. Studies reveal that the stroke in HIV patients is increasing even in the general population from stroke data.
Material and methods: The cross sectional study was conducted in the Department of General Medicine, Belagavi Institute of Medical Sciences Belagavi, India. Twenty HIV infected patients fulfilling inclusion criteria, were included and a detailed history of mode of transmission of HIV, risk factors, Laboratory investigation findings was noted.
Results: Twenty HIV infected stroke patients were included in the study, 12 were males & 8 were females.The mean age at presentation was 41.15 with SD 13.05565. Patients had risk factors like age, menopause, alcohol, diabetic, smoking, dyslipidemia. Seventy five percent females had menopause as risk factors and 30% patients had dyslipidemia as risk factor. Forty five percent patients were presented during initial 1 year after HIV infected status and 25% patients were presented 1-2 year after HIV infection. The median CD4 counts at presentation was 139.
Conclusion: HIV infection is one of the risk factor for the occurrence of stroke in young population, due to exposure to opportunistic infections. Chronic inflammation due to HIV infection results in a prothrombotic state. HIV/ART-induced dyslipidemia may lead to etiopathogenesis for stroke.

Keywords: stroke, HIV, risk factors, opportunistic infections

Introduction

According to recently released report, India HIV Estimation 2015 report, HIV prevalence in adult (15–49 years) is 0.26% (0.22% – 0.32%) estimated in 2015 [1]. HIV prevalence among males is 0.30% and among Females is 0.22% estimated. The prevalence of HIV in Karnataka state is 0.45%. The highest HIV prevalence is in Manipur state of 1.15% estimated.

According to the World Health Organization criteria stroke is defined as a clinical syndrome consisting of an abrupt onset of a focal neurological deficit that is attributable to a focal vascular cause. The symptoms lasting > 24 hours or leading to death before this period with no other cause than cerebrovascular disease [2]. Sub arachnoid hemorrhage and transient ischemic attack patients were excluded from this definition. Cerebral infarction and Intra-Cerebral Hemorrhage (ICH) definitions were based on the criteria of the Stroke Data Bank of the National Institute of Neurological Disorders and Stroke [3].

The burden of both communicable and non-communicable diseases are more prevalent in developing countries like India. Stroke is one of the leading causes of death and disability in India. The estimated adjusted prevalence rate of stroke range, 84-262/100,000 in rural and 334-424/ 100,000 in urban areas [4].

Stroke in HIV is increasing in the developed countries from the data & studies. To say HIV infection as one of the risk factor for stroke is not known and the mechanism still being unclear [5]. In 2004 Cole JW *et al.* published the first population-based study, showed that HIV is strongly associated with both ischemic and hemorrhagic stroke.[6] Several mechanisms have been proposed for association of stroke in HIV: HIV infection causing a pro-thrombotic state[7] or HIV-induced vasculopathy [8, 9] or in the conditions of infections or meningitis.

HIV is an emerging etiology for stroke in the young, particularly in a population with high seroprevalence for retroviruses. Studies reveal that the stroke in HIV patients is increasing even in the general population from stroke data. Presentations where stroke as the first manifestation of HIV infection is not unheard of in the present day clinical practice, furthermore stressing the importance of this topic.

Aims &Objectives

Aim: To study the association of stroke in human immunodeficiency virus infected patients

Objectives

1. To study the association of risk factors of stroke among the HIV patients admitted in BIMS Hospital, Belagavi.
2. To study the correlation between CD4 count, opportunistic infections (syphilis, tuberculosis & toxoplasmosis) & Computed Tomography (CT) brain findings.

Materials and methods

The cross sectional study was conducted in the Department of General Medicine, Belagavi Institute of Medical Sciences

Belagavi, during the period from July 2017 to November 2017. The approval from the institutional ethical committee was taken. All the procedures were followed in accordance with Helsinki declaration 1975 which was revised in 2013.

HIV infected patients aged between 15 – 65 years admitted to BIMS, hospital Belagavi during the period from June 2016 to June 2017 were included in the present study. Twenty HIV infected patients presented with stroke were included in study. Detailed basic information of all the patients such as their age, sex, date of admission (DOA) was recorded. A detailed history of mode of transmission of HIV, risk factors for stroke like smoking, alcohol, type 2 diabetes mellitus, hypertension, cardiac disorders (valvular heart disease and cardiomyopathies) and bleeding diathesis was recorded. Laboratory investigation findings such as Random Blood Sugar, Renal Function Test, Liver Function Test, lipid profile, Complete Blood Count, HIV ELISA (Enzyme Linked Immuno Sorbent Assay), Western blot, CD4 cell count, Venereal Disease Research Laboratory (VDRL), Coagulation profile, Cerebro Spinal Fluid (CSF)examination, Urine examination, Chest X ray, Electrocardiograph (ECG), Echocardiography, Carotid Doppler study, CT brain, MRI report was noted. Patients were also screened for hepatitis B virus (HBV) and hepatitis C virus (HCV) co-infections. HIV status of all the patients was confirmed as per National AIDS Control Organization (NACO) guidelines such as ELISA & western blot techniques. CD4 cell count by fluorescence activated cell sorter (FACS) method was considered to assess the severity in every patient. An enquiry into the patient's Anti Retroviral Therapy (ART) regimen and duration was noted from records. The HIV patients with age >65 years, hypertension, atrial fibrillation, is hemic heart disease, familial dyslipidemias, obesity was excluded from the study

A final diagnosis of stroke was made with the corroborative evidence from clinical examination findings and investigation data such as. MRI, CT brain. WHO definition of Stroke was used for final diagnosis [10].

Statistical analysis: The data was presented as mean ± SD, percentage values. P value of ≤ 0.05 will be considered for statistical significance.

Table 1: Distribution of HIV patients with respect to stroke

	Parameter	Number of patients (n=20)	Percentage
Risk factors	Menopause*	6	75
	Alcohol	4	20
	Diabetic	2	10
	Smoking	2	10
	Dyslipidemia	6	30
Duration of HIV (in years)	<1	9	45
	1-2	5	25
	2-4	2	10
	>4	4	20
Opportunistic infections	Tuberculosis	6	30
	P.Carini Pneumonia	2	10
	Others	2	10
ART regimen	TLE	10	50
	ZLN	8	40
	Not started	2	10

*n=8

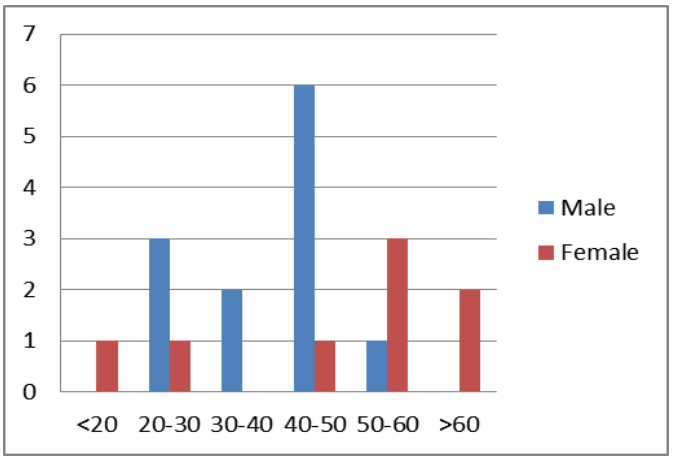

Fig 1: Age and sex wise distribution of patients

Results

Twenty HIV infected stroke patients were included in the study, 12 were males & 8 were females. The mean age at presentation was 41.15 with SD 13.05565. According to graph 1, the age & sexwise distribution of patients maximum males were presented during 40-50 years age group & females were presented during 50-60 years age group. Patients had risk factors like age, menopause, alcohol, diabetic, smoking, dyslipidemia. Seventy five percent females had menopause as risk factors and 30% patients had dyslipidemia as risk factor. Forty five percent patients were presented during initial 1 year after HIV infected status and 25% patients were presented 1-2 year after HIV infection. The median CD4 counts at presentation was 139. Thirty percent patients were presented tuberculosis as opportunistic infection followed by P.Carinii pneumonia in 10 %.t Other opportunistic infection were present in 10% patients namely Kaposi sarcoma & Cryptococcus neoformans. Eighteen patients were on ART treatment, ZLN (Zidovudine +Lamivudine +Nevirapine) regimen in 10 patients & TLE (Tenofovir +Lamivudine +Efavirenz) regimen in 8 patients.

Discussion

In our study the mean age of occurrence of stroke in HIV patients is 41.15 years which is earlier than HIV negative

patients in general population. This is due to exposure to opportunistic infections, HIV/ART-induced dyslipidemia, which is supported by Benjamin LA *et al*. study, that revealed at a population level, studies in developed countries have consistently shown that HIV-infected individuals have a substantially high risk of stroke, roughly equivalent to that of general population cohorts 10–20 years older than themselves. [11] HIV could have a causal role in this disease mechanism, but this is still open to debate. However, there is growing evidence that HIV-related chronic inflammation even in well-suppressed HIV-infected individuals is linked to subclinical vasculopathy

In our study opportunistic infections were presented in 50 % cases. The mean CD4+ cell count 152.4 was found in our study. Deshapande *et al*. study revealed, 29.8% of non-OI manifestations were stroke syndromes. Ten patients (50%) had a CD4+ cell count between 200 and 500 cells/mcL, whereas 8 cases had a CD4+ cell count between 100 and 200 cells/mcL. The mean CD4+ cell count in the study was found to be 212 cells/mcL. Seventy-five percent of the patients had stroke in young, because of prothrombotic state from HIV infection [12]. This prothrombotic state is due to a complex mix of effects of anticardiolipin antibodies, low protein S levels, and altered heparin cofactor II levels. In addition to this, vasculitis produced by the virus itself tends to be prothrombotic due to the endothelial dysfunction, resulting in a significant overlap between the two.

In our study all 20 cases were presented with ischemic stroke. Ovbiagele and Nath[13]reported that ischemic stroke was the predominant pathological stroke type and that the proportion of patients with ischemic stroke among those with HIV doubled between 1997 and 2006. Whether this rise is a result of cart or methodological factors is not clear.

Conclusion

HIV infection is the major contributory risk factor for the occurrence of stroke in young population, due to exposure to opportunistic infections namely tuberculosis, Cryptococcus cause vasculitis. Chronic inflammation due to HIV infection results in a prothrombotic state. HIV/ART-induced dyslipidemia may lead to etiopathogenesis for stroke. The incidence of stroke in HIV increases with decrease in CD4 count due to opportunistic infections, inflammation. Larger population based age and sex matched and outcome studies are needed to strengthen the etiological association as well as HIV- associated stroke.

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