ORIGINAL RESEARCH PAPER

General Medicine

DIFFERENT TYPES OF NEUROLOGICAL MANIFESTATIONS IN PATIENTS WITH HIV INFECTION AND THEIR CORRELATION WITH THE CD4 COUNT AT A TERTIARY CARE CENTER OF ODISHA.

KEY WORDS: CD4 count, the neurological manifestation of HIV.

Dr. Sarat Chandra Singh M.B.B.S. AND M.D., General Medicine Assistant Professor, P. G. Department Of Medicine, S. C. B. Medical College, Cuttack, Odisha, India. Pin-753003,

Dr. Madhusmita Patnaik M.B.B.S. AND M.D., General Medicine, Assistant Professor, P. G. Department Of Medicine, S. C. B. Medical College, Cuttack, Odisha, India. Pin-753003,

Dr. Gautam Patnaik MBBS AND MD Microbiology, Research Associate, Special Center For Molecular Medicine, Jnu, New Delhi, India.

Dr. Dipti Ranjan Tripathy Junior Resident, General Medicine, P. G. Department Of Medicine, S. C. B. Medical College, Cuttack, Odisha, India. Pin-753003,

ABSTRACT

INTRODUCTION: Neurological disorder due to HIV infection develops in more than 50% of individual in the world today. The present study had designed for neurological manifestations and their co-relation with CD4 count.

METHODS: Fifty consecutive naive HIV/AIDS patients were included in the study. Detailed clinical history and all tests were done including CD4 count. Exclusion criteria were HIV/AIDS patients on antiretroviral therapy, history of epilepsy, CVA, head injury, psychiatric illness, Parkinsonism and diabetes mellitus.

RESULTS: The study showed tubercular meningitis in 30% of cases, tuberculoma 4%, cryptococcal meningitis in 20% cases and neuropathy in 14% cases. The mean CD4 count was 137.38+7.93/mm^3 in tubercular meningitis and 68/mm^3 in cryptococcal meningitis and toxoplasmosis, which was extremely significant (P value< 0.0001).

CONCLUSION: Most neurological manifestations and opportunistic infections were documented with CD4 count below 200/mm^3.

INTRODUCTION:

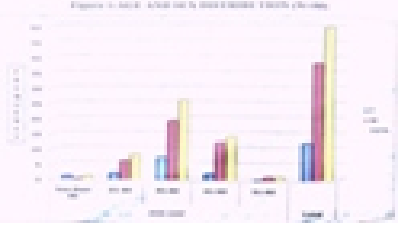
HIV is one of the fastest growing health problems in the world today [(1)]. The world health organization (WHO) estimates that 40 million people in the world are infected with HIV. Approximately 95% of cases, as well as most deaths from AIDS, occur in the developing countries. India has the 2nd largest burden of HIV infection, next to sub-Saharan Africa [(2)]. In 2009 approximately 2-4 million people were estimated to be living with HIV/AIDS in India, (AIDS epidemic updates, 2010). Children (< 15 years) account for 3.5% for all infection, while 83% are in the age group 15 to 49 years. The estimated adult HIV prevalence in India was 0.3% in 2009. India had approximately 0.12 million new HIV infection in 2009 (NACO 2010) [(3)]. The neurological disorder develops in more than 50% of individuals infected with HIV. Also, neuropathological lesions are detected at autopsy in approximately 90% of cases. This may be explained by the fact that the central nervous system is a sanctuary site for HIV and there is poor penetration of antiviral drugs due to the presence of the intact blood-brain barrier [(4)]. Among all organs, the nervous system is the most frequent and serious target of HIV infection occurring in patients with profound immune suppression. The cerebrospinal fluid finding is abnormal in about 90% of patients even during the asymptomatic phase of HIV infection [(5)]. HIV Sentinel Surveillance in 2007 was detected that neurological disorder is the 1st manifestation of Symptomatic HIV infection in 10 -20% of patients [(1)]. The neurological manifestation may be either primary to a pathological process of HIV infection or secondary to opportunistic infection or neoplasm. It may be inflammatory demyelinating or degenerative in nature [(5)]. The neurological manifestations, natural course and outcome of HIV disease is likely to be different in India from other countries [(1)]. The present study is designed to assess the various neurological manifestations in the patient with HIV infection and their co-relation with the patient's CD4 count.

METHODS:

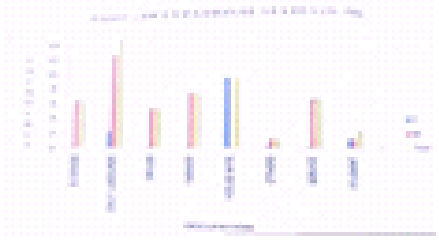
Our aim is to study various neurological manifestations in patients with HIV infection and to correlate Neurological manifestations with their CD4 count. Fifty consecutive naive HIV / AIDS patients with neurological complications in different stages of disease were included in the study. Detailed clinical history and neurological examination, all routine blood count, biochemical blood test, CSF analysis (Total cell count, Differential count, Gram stain, AFB stain, Indian Ink stain for Cryptococcus, sugar, protein, ADA, VDRL, (Slide flocculation method) culture for cryptococcus were done. Other diagnostic investigation like HSV- I/II IgM and IgG (Enzyme immune assay), toxoplasma serology (illuminiscent microparticle immune assay method), MRI / CT of Brain and Electro-physiological studies like nerve conduction study were done.Inclusion criteria were all newly diagnosed cases to be HIV +ve were included in the study.The cases of HIV / AIDS already on HAART, H/o Epilepsy, CVA, Head injury, Psychiatric illness, parkinsonism, and diabetes mellitus were excluded from the study.Statistical analysis of the data was done using a software SPSS-20.0. Microsoft word and excel had been used to generate graphs and tables.

RESULTS:

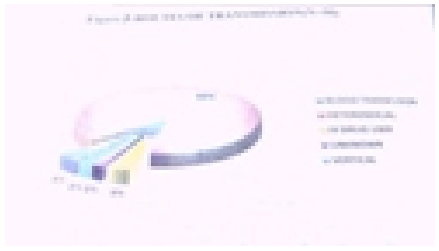
Fifty cases, of naive HIV/AIDS patients with neurological manifestations in different stages of disease admitted to the hospital, were studied. Out of these 38(76%) cases, were male and 12(24%) were female in gender. This was correlated with the study done by Sircar et al[(6)] and NACO 2010[(3)]. 90% of patients were between 15-45 years of age and correlated with the study done by Snyder et al[(7)]. Mean age for males were 36.95yrs and for females were 38yrs.This was concordance with the study done by Mc.Arthur et al[(8)]. It is showing in figure-1.



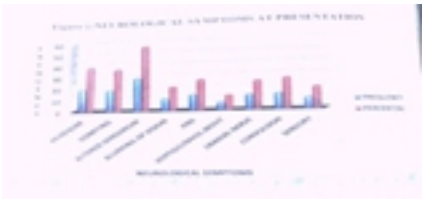
Comparing urban to the rural area, 52% of patient belongs to rural areas. 28% of patients were the daily laborer, 14% were farmers, service holder and businessman 12%, driver 15%, rest 46% of patient had the history of migration to other states for their livelihood.Nearly same results were studied by Mohan et al, Rajsekaran et al and Devi SB et al.(9,10,11). It is showing in figure-2.



In this study, the common mode of acquisition of HIV infection was the heterosexual route in 88% of patients, IV drug abusers were 4% and vertical was 2%. This is correlated with other studies(3,9,10,11,12) . It is showing in figure-3.

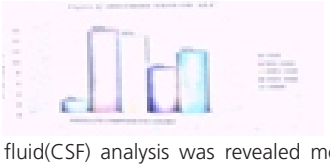


Fever (76%) and weight loss(38%) were the commonest symptoms other than neurological symptoms in this study. Altered sensorium was the most common neurological symptoms seen in 29 (58%) of patients, then a headache in 38%, Vomiting in 18% and other symptoms were seen i.e. seizures, paresthesia and limb weakness.This was comparable to the study done by Wadia RS, Pujari SN et al (13), they documented neurological symptoms in 30% of their patients. It is showing in figure-4.



Higher mental function impairment was the commonest neurological sign i.e. 58% followed by the meningeal sign in 44%. Cranial nerve involvement and fundal abnormalities each composed 25%. Papilloedema was the commonest finding in 20%, and extensor plantar response was seen in 66% of cases. It is showing in figure-5.

Mean absolute lymphocyte count(ALC) was 1684.44 cells/microliter ranging from 407 to 7821. Mean count in cryptococcal meningitis was 1340 cells/microliter and for central nervous system tuberculosis(CNS-TB), it was 1547 cells/microliter. It is showing in figure-6.



Cerebrospinal fluid(CSF) analysis was revealed most cases had predominant lymphocytes, a mean protein was 90.68mg/dl for all cases but average protein was 113.64mg/dl in cases of TBM, the sugar range was 41-70mg/dl in cases of CNS –TB and below 40mg/dl in pyogenic and cryptogenic meningitis. It is showing in figure-7.

CT/MRI of the brain had found that hydrocephalous in 10% cases, all were TBM, Cerebral edema was found in 6%, space occupying lesion of brain in 6%, Cerebral atrophy in 2%, haemorrhage in 2%, periventricular infarcts in 2% and other infarcts in 8%. In 32% of patients, the imaging studies were normal. It is shown in figure-8. All had similar with the results by other studies[4,7,8,13,14,15].

Most of the patients were presented with stage III / IV of HIV/AIDS infection. A high proportion of patients had an AIDS-defining illness as this was an inpatient based study. According to the neurological diagnosis, tubercular meningitis(TBM) was the commonest manifestation seen in 30% cases, 20% cases were cryptococcal meningitis, 4% had toxoplasmosis. 2% case had co-existent tubercular & cryptococcal meningitis. CVA was found in 8 patients out of 7 had infarcts and one had the intracerebral bleed. Seven patient had HIV induced Neuropathy. This is also concordance with other studies [4,7,8,13]. It is showing in figure-9.

The mean CD4 count was detected around 164.14/mm3 for all cases(1). 60% cases had CD4 counts less than 200/mm3 whereas only 40% cases had more than 200/mm3(13). It is showing in table-1.

Mean CD4 counts in males were 152.68/mm3 and female were 200.42/mm3 and mean absolute lymphocyte count(ALC) in males were 1737.37cells/microliter and in females were 1516.83cells/microliter respectively and this is statistically more significant(P=<0.0299). Tubercular meningitis was associated with the CD4 count of 137.38+_79.93/mm3, Cryptococcal Meningitis and toxoplasmosis both were associated with a mean CD4 count of 68/mm[3(1,16,17)]. As it is shown in table-2.

Correlation of CD4 count Vs ALC in various neurological diseases, in HIV/AIDS, was extremely significant (P-value <0.0001). Peripheral nerve involvement and CVA were associated with a higher CD4 count inferring that they are not the AIDS-defining illness.This is correlated with the literature available [13]. It is showing in figure-10.

CONCLUSION:

CSF examination reveals a positive diagnosis in the majority of patients. Meningitis was the commonest secondary neurological manifestation (>50%) comprising 15 cases of tubercular meningitis, 10 cases cryptococcal meningitis. Other common neurological manifestation includes peripheral neuropathy, CVA, pyogenic meningitis, HIV encephalopathy, CNS toxoplasmosis, HSV encephalitis. Co-existent of tubercular meningitis with cryptococcal meningitis was found, which need for the physician to be aware of the existence of multiple opportunistic infections in one patient. Neuro-imaging studies and CSF analysis are useful in diagnosing opportunistic infection of the Nervous system. CD4 count co-related better with the degree of immune suppression and with various neurological manifestations. Patient in WHO stage IV HIV/AIDS infection was at maximum risk of neurological complications. CD4 counts were significantly lower in patients with most neurological complication and most of the opportunistic infections were documented in the patient with CD4 count < 200/mm^3. The study also established that in spite of good CD4 count, there was an increased risk of neurological complication as seen with peripheral neuropathy.A Higher index of suspicion is necessary to detect HIV patient presenting with neurological symptoms to diagnose and treat the underlying cause.

BIBLIOGRAPHY:

1. Patel M.L., Sachan R., Atam V., Chaudhury S.C., and Gupta A., Various neurological manifestations in HIV positive patients,their outcome and correlation with CD4 counts-A tertiary center experience in North Indian population: Journal of AIDS and HIV Research:2012; vol.;4(7);198-202.
2. Global report, UNAIDS report in AIDS Epidemic 2010.
3. National AIDS control Organisation. A press release on HIV estimates 2009.
4. Levy R.M., Bredesen D.E., Rosenblum M.L.; Neurological manifestations of the acquird immunodeficiency syndrome(AIDS): experience at UESF and review of literature: Journal of neurosurgery 1985:62(4);475-495.
5. Fausi S.A., Lane C.H.: Human Immunodeficiency Virus Disease: AIDS and related disorders: Harrison's Principles of Internal Medicine: 18th Edison:2010:1506-68,1852-1913.
6. Sircar A.R., Tripathi A.K., Choudhury S.K., Misra R.: Clinical profile of AIDS: a study at a referral hospital: Journal of association of physicians of India:1998;46(9):775-8.
7. Snider W.D., Simpson D.M., Neilsen S., Gold J.W., Metroka C.E., Posnel J.E.: Neurological complications of acquired immune deficiency syndrome: analysis of 50 patients; Ann Neurol.1983;14(4):403-18.
8. McArthur IC, Neurologic manifestation of AIDS, Medicine(Baltimore) 1987;66: 407.37.
9. Mohanty K.C., Sundrani R.M.: HIV infection and AIDS in the developing world: BMJ.2001;vol.322: 16: 40:5.
10. Rajsekharan R., Lima A., Kamakshi S., Jayaganesh D., Senthamighehelvan A., Savithan S., et al: Trend of HIV infection in patients with tuberculosis in rural south India:Indian Journal of Tuberculosis. 2000; 47: 223.
11. Devi S.B. Naorem S., Singh K.B.,Prasad L.,Devi T.S.: HIV and TB co-infection. A study from RIMS Hospital.Manipur:Journal of Indian Academy Clinical Medicine. 2005;6:220-3.
12. John T.J., Babu P.G. Saraswathi N.K., Jayakumari H., Selvaraj R.,Kaur A., et al: The epidemiology of AIDS in the Vellore region, South India. AIDS. 1993; 7(3):421-4.
13. Wadia RS, Pujari SN,Kothari S, et al. Neurological manifestation of HIV disease, API 2001; 49:343-8.
14. Puccioni M. Favorets A.C., Andre C., Peirots C.A., Novis S.A.: acquired immunodeficiency syndrome: analysis of neurologic complications in 44 cases: A J neuropsychiatry: 1989: 47(4): 385-91.
15. Satishchandra P, Nalini A. Gourie-Devi M, Khanna N, et al profile of neurological disorders associated with HIV/AIDS from Bangalore.(1989-1996) Indian J Med Res 2000:111:14-23.
16. Sanchez P.J., Perez C.E., Jimenez E.A., Martin R.P., Roca V., Ruiz Y.M.,et al: Tuberculos Meningitis. Clinical charecteristics and comparison with cryptococcal meningitis in patient with human immunodeficiency virus infection. Arch Neurol: 1996: 53(7): 671-6.
17. Crowe SM, Carlin J.B, Stewart KI, Lucas CR, Hoy JF. predictive value of CD4 lymphocyte numbers for the development of opportunistic infections in HIV infected persons. AIDS 1991,4(8):770-6.