RESEARCH ARTICLE

Clinical profile of neurological manifestations of human immunodeficiency virus patients- A tertiary hospital- Descriptive study

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Vyas Y, Vyas M, Sanwalka M. Clinical profile of neurological manifestations of human immunodeficiency virus patients- a tertiary hospital- cross sectional study. Int J HIV AIDS Res. 2022; 6(3):1-4.

ABSTRACT

Background: Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS) is a global pandemic. As per the UNAIDS report on global AIDS epidemic 2020 globally, an estimated 38.0 (31.6–44.5) million people were living with HIV in 2019. The current Centers for Disease Control and Prevention (CDC) classification system for HIV infected adolescents and adults categorize persons based on the clinical conditions associated with HIV and CD4 counts. Using this system any HIV infected individual with a CD4 count of less than 200/mm^3 has AIDS by definition regardless of the presence of symptoms or opportunistic diseases. A decrease in CD4 count leads to various Opportunistic Infections (OIs) in these patients and serious manifestations related to HIV.

Materials and Methods: This was a tertiary hospital based cross sectional study of 101 cases. All HIV positive patients with neurological signs and symptoms irrespective of age were included in this study. Patients who had HIV-unrelated developmental, neurological, medical, and neurobehavioral conditions that impaired cognition were excluded from this study A detailed history of patients like age, sex, address, family history, mode of transmission, treatment history and history of coexisting illness were taken and entered in proforma. A thorough examination and other routine and special investigations like ELISA (enzyme-linked immunosorbent assay) and CD4 count were done.

Results: In the present study 73 cases (72.27%) belonging to age group 30 years to 49 years were affected, followed by 15years-29years of age group. 81 cases (80.19%) of males were affected, followed by 20 cases (19.80%) of females. Out of 101 patients 74 cases (73.26%) had history of long standing fever and 27 cases (26.73%) had negative history. 85 cases (84.15%) had persistent cough for more than a month, while 16 cases (15.84%) had negative history. 36 cases(35.64%) had history of diarrhea for more than 1 month, and 65 cases (64.35%) had absence of such history. 89 cases (88.11%) had history of unexplained weight loss, and 12 cases (11.88%) had no such history. Tuberculous Bacterial Meningitis (TBM) was the most common manifestation in 32 cases (31.68%), viral encephalitis in 15 cases (14.85%), cryptococcal meningitis in 14 cases (13.86%). Progressive Multifocal Leukoencephalopathy (PML) was the least common manifestation seen in 1 case (0.99%) only. Present study had 78 cases (77.22%) of WHO stage 4 cases and 23 cases (22.77%) of stage 3.

Conclusion: In conclusion this study emphasizes the fact that tuberculosis and cryptococcus infections are the frequent opportunistic infections associated with HIV. There is a direct correlation between CD4 count and severity of infection, hence indicate level of immunity and disease. It also shows that various neurological manifestations are due to these opportunistic infections. This dual course of HIV and tuberculosis infection should be controlled by providing awareness of the disease transmission, progression and prevention. Due to high cost of Anti-Retroviral Drugs (HAART) and low availability of HIV centres, patients lack access to proper treatment which inturn leads to development of opportunistic infections in later course of disease. CD4 counts is important in managing specific therapy for HIV-positive patient.

Key Words: *Opportunistic infection; HIV positive; Tuberculosis; Cryptococcus; CD4 cells*

INTRODUCTION

HIV/AIDS is a global pandemic [1]. As per the UNAIDS report on the global AIDS epidemic in 2020 globally, an estimated 38.0 (31.6–44.5) million people were living with HIV in 2019.2 There were 1.7 (1.2–2.2) million new HIV infections globally, showing a 23% decline in the number of new infections from 2.1 (1.6–2.9) million to 1.7 (1.2-2.2) million in 2019.2 At the same time the number of AIDS-related deaths has been reduced by 60% since the peak in 2004. In 2019, 6,90,000 (5,00,000- 9,70,000) people died from AIDS-related illness worldwide, compared to 1.7 (1.2-2.4) million people in 2004 and 1.1 million people in 2010 [2].

South and South East Asia are the second most affected, in 2010 this region contained an estimated 4 million cases or 12% of all people living with HIV resulting in approximately 250,000 deaths [3]. Approximately 2.4 million of these cases are in India [3]. In 1983, HIV was isolated from a patient with lymphadenopathy, and by 1984 it was demonstrated as a causative agent of AIDS. The first case of this disease was detected in the year 1986 in India. Various data show a high prevalence of HIV in states like Manipur, Andhra Pradesh, Mizoram, Nagaland, Karnataka, and Maharashtra. HIV/AIDS has become a chronic rather than an acutely fatal disease in many areas of the world [4]. Prognosis varies between people, and both the CD4 count and viral load are useful for predicting outcomes.

The current CDC classification system for HIV-infected adolescents and adults categorizes persons based on the clinical conditions associated with HIV and CD4 counts. Using this system any HIV-infected individual with a CD4 count of less than 200/mm^3 has AIDS by definition regardless of the presence of symptoms or opportunistic diseases [5]. Without treatment, the affected survival time after infection is approximately 9 years-10 years depending upon the HIV subtypes [6].

The important causes of death from HIV/AIDS are opportunistic infections and cancers both of which are frequently the result of the progressive failure of the immune system [7,8]. These opportunistic infections are a common complication of HIV infection which causes morbidity, hospitalization, expensive therapy, and decreases the life span of an individual. Tuberculosis co-infection is one of the leading causes of sickness and death in patients with HIV/AIDS and causes 25% of HIV-related deaths [9].

Up to 70% of infected individuals have neurological symptoms, and meningitis is the cause of HIV-related mortality and morbidity in a maximum number of patients [10]. In India, according to some studies tubercular meningitis is the most common neurological manifestation in HIV patients, followed by *cryptococcus meningitis.*

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Received: April 28, 2022, Manuscript No. pulijhar-22-5201; Editor Assigned: May 02, 2022, PreQC No. pulijhar-22-5201 (PQ); Reviewed: May 12, 2022, QC No. pulijhar-22-5201 (Q); Revised: May 17, 2022, Manuscript No. pulijhar-22-5201 (R); Published: May 26, 2022, DOI: 10.37532/ pulijhar.2022.6(3).01-04

A decrease in CD4 count leads to various OIs in these patients. The introduction of ART has reduced OIs incidence but initiation and maintenance of therapy are dependent on CD4 count. The primary target of HIV pathogen is the cell-bearing CD4 marker on their surface. As HIV infection increases, there is a gradual loss of cells bearing CD4 antigen receptors (most important are T helper cells), B lymphocytes, and natural killer cells. This leads to the development of OIs and other serious manifestations related to HIV. Hence, the present study was undertaken to find the prevalence of various neurological manifestations in HIV-positive diagnosed patients and correlate it with CD4 count and WHO staging. The WHO systems for adults sort patients into one of the four clinical stages [11].

Clinical stage 1-consists of asymptomatic patients and those with persistent lymphadenopathy.

Clinical stage 2- Moderate unexplained weight loss, Recurrent respiratory tract infections, Herpes zoster, Angular cheilitis, Fungal nail infection, Recurrent oral ulcerations.

Clinical stage 3- Unexplained severe weight loss, Unexplained chronic diarrhea for longer than 1 month, Unexplained persistent fever (intermittent or constant for longer than 1 month), Persistent oral candidiasis, Unexplained anemia (below 8 g/dl), neutropenia (below 0.5×10 9/l) and/ or chronic thrombocytopenia (below 50×10 9 /l)

Clinical stage 4- HIV wasting syndrome (weight loss>10% of body weight, plus either unexplained diarrhea for more than 1 month or chronic weakness), Pneumocystis jiroveci pneumonia, Oesophageal candidiasis (candidiasis of trachea, bronchi, or lungs), Extrapulmonary tuberculosis, *Kaposi sarcoma*.

AIMS AND OBJECTIVES

The aims and objectives of the present study were:

- To study the clinical Profile Of Neurological Manifestations Of Human Immunodeficiency Virus Patients
- And their correlation with the WHO staging and $CD4^+$ cunt

MATERIAL AND METHOD

This was a tertiary-based cross-sectional study of 101 cases.

Inclusion Criteria

- All HIV-positive patients with neurological signs and symptoms irrespective of age were included in this study.

Exclusion Criteria

- Patients who had HIV-unrelated developmental, neurological, medical, and neurobehavioral conditions that impaired cognition were excluded from this study.

A detailed history of patients like age, sex, address, family history, mode of transmission, treatment history, and history of coexisting illness was taken and entered in the proforma. A thorough examination and other routine and special investigations like ELISA (Enzyme-Linked Immunosorbent Assay) and CD4 count were done. Informed consent was taken from each patient before the study and ethical committee approval was taken. (NIMSUNI/IEC/2018/0987)

RESULT

Out of 101 patients, 74 cases (73.26%) had a history of long-standing fever and 27 cases (26.73%) had negative history. 85 cases (84.15%) had a persistent cough for more than a month, while 16 cases (15.84%) had negative history. 36 cases (35.64%) had a history of diarrhea for more than 1 month, and 65 cases (64.35%) had an absence of such history. 89 cases (88.11%) had a history of unexplained weight loss, and 12 cases (11.88%) had no such history Figures 1 and 2, Table 1.

All the patients presented with abdominal pain. This abdominal pain was worse on lying supine and relieved by sitting upright. Other presenting symptoms are shown Table 2.

In the present study most common symptom was headache (80.19%), followed by seizures (23.76%) and behavior changes (15.84%) Table 3. 81 cases (80.19%) had CD4 count<200/mm^3 and 20 cases had CD4 count between 200/mm^3-500/mm^3 Table 4. TBM was the most common manifestation in 32 cases (31.68%), viral

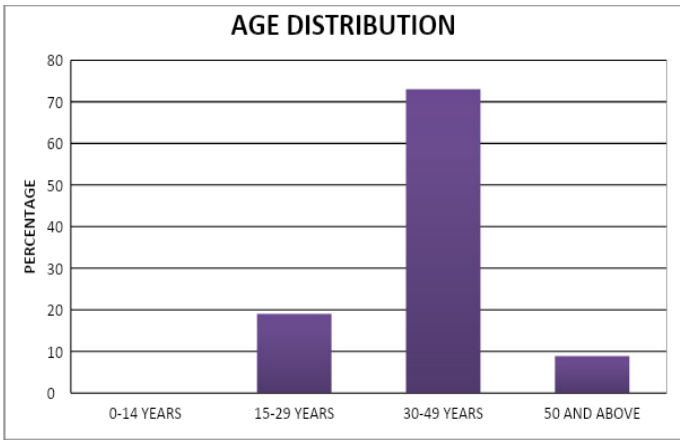

Figure 1) *Graph showing the Age distribution of patients*

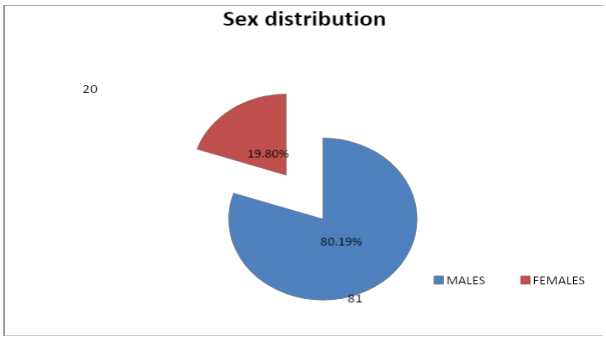

Figure 2) *Graph showing sex distribution of patients*

TABLE 1
Distribution of patients according to the mode of transmission.

Mode of transmission	Percentage of the patient (%)
HIV Partners	80%
HIV mother	5%
Blood transfusion	4%
Unknown	11%
Total	100%

TABLE 2
Distribution of patients according to symptoms

Symptoms	Present (cases)	Not present (cases)
Fever >1 month	74	27
Cough	16	85
Diarrhea>1 month	36	65
Unexplained weight loss	89	12

TABLE 3
Distribution of patients according to various neurological manifestations

Symptoms	Number of patients	Percentage (%)
Dizziness	7	6.93%
Fainting	6	5.94%
Headache	81	80.19%
Bowel bladder incontinence	13	12.87%
Memory impairment	2	1.98%
Numbness	2	1.98%
Seizures	24	23.76%
Speech difficulties	5	4.95%
Tremors	0	0%
Loss of coordination	0	0%

Loss of concentration	2	1.98%
Painful blisters	0	0%
Itching, tingling	2	1.98%
Painful burning sensation	0	0%
Unsteady gait	3	2.97%
Behavior changes	16	15.84%
Vertigo	11	10.89%
Lower limb weakness	12	11.88%
TOTAL	101	100%

TABLE 4
Distribution of cases according to CD4 count

CD4 count	Number of cases (n-101)	Percentage (%)
<200	81	80.19%
200-500	20	19.80%
>500	0	0%

TBM- Tubercular Bacterial Meningitis; HBV- Hepatitis B Virus; Toxo-Toxoplasmosis; PML- Progressive multifocal leucoencephalopathy; SOL-Space occupying lesion

TABLE 5
Distribution of cases according to CD4 count

CNS manifestation	No of patients	CD4 count	
		<200/mm³	200/ mm³-500/mm³
Cryptococcus	7 (6.9%)	7	
Cryptococcus+oral candidiasis	5 (4.9%)	5	
Cryptococcus + TBM	1 (0.99%)	1	
Cryptococcus + Hydro-cephalus	1 (0.99%)	1	
TBM	15(14.85%)	8	7
TBM +Oral candidiasis	5 (4.95%)	2	3
TBM +HBV	4 (3.9%)	1	3
TBM +Encephalitis	2(1.9%)	2	
TBM +Hydrocephalus	4(3.9%)	4	
Toxoplasmosis	5(4.95%)	5	
Pyogenic Meningitis	4 (3.9%)	2	2
Fungal meningitis	2 (1.9%)	1	1
Viral encephalitis	12 (11.88%)	12	
Toxo + encephalitis	1 (0.99%)	1	
Cerebritis	4 (3.9%)	4	
Undiagnosed	5 (4.95%)	3	2
Cerebral atrophy	5(4.95%)	5	
Cerebellar demylination	3 (2.97%)	3	
Cerebral infarct with hemiplegia	3 (2.97%)	3	
HBV + Oral candidiasis	1(0.99%)		1
HAD(HIV-associated dementia)	4(3.9%)	4	
PML	1(0.99%)	1	
Hydrocephalus	3(2.97%)	3	
TBM+oral candidiasis+HBV	1(0.99%)	1	
SOL	3(2.97%)	3	

TABLE 6
WHO staging of patients

WHO stage	No of the patients (n-101)	Percentage (%)
STAGE 3	23	22.77%
STAGE 4	78	77.22%

encephalitis in 15 cases (14.85%), and cryptococcal meningitis in 14 cases (13.86%). PML was the least common manifestation seen in 1 case (0.99%) only Table 5. The present study had 78 cases (77.22%) of WHO stage 4 cases and 23 cases (22.77%) of stage 3 Table 6.

DISCUSSION

HIV has a great impact on society, both as an illness and as a source of discrimination. The disease also has an economic impact. Approximately 2.4 million HIV cases are in India itself [12]. The estimated prevalence of nervous system disorders among patients receiving highly active anti-retroviral therapy but also requiring neurological care is over 25% [13].

In this study, it was found that fever was the most frequently occurring symptom present in 74% of the patients followed by weight loss (89%), diarrhea (36%), and cough (16%). These findings are consistent with studies of Ramesh et al, Boruah et al and Korzeniewska-Kosela [14-16]. Due to decrease immunity in HIV-positive patients, various opportunistic infections develop. In the present study, it was found that TBM was the most common manifestation (31.68%) followed by viral encephalitis (14.85%), and cryptococcal meningitis (13.86%). PML was the least common manifestation seen in 1 case (0.99%) only. This is similar to the study done by Sharma et al, Vajpayee et al, and Ramesh et al [14,17,18]. Whereas contradictory to the study of Gaud et al, Giri et al, and Singh et al [19-21] which showed candidiasis as the most common followed by TB.

The present study reported headache as the most common neurological manifestation in 80 cases (81.18%) which correlated with another study by Bolokadze N et al also [22]. Even in patients without overt focal brain dysfunction, headache can be a presenting symptom of focal parenchymal diseases when they involve "non-eloquent" brain areas or are characterized by small multifocal lesions. However, when CNS dysfunction is truly absent, headache most commonly relates to either meningitis or a poorly understood condition sometimes referred to as HIV headache [23].24 cases (23.76%) with seizures, which is in concordance with the studies done by Sonkar et al, N Bolokadze et al. Pal et al, and Holtzman DM et al. [22,24-26] reported 33% and 32% cases with new onset of seizures respectively.

Our study shows that in neurologically manifested HIV patients, tubercular meningitis manifested more than cryptococcal meningitis which is similar to a study done by Sonkar et al. [24]. Other studies also reported tubercular meningitis to be present in 43.8% versus 28.1% and 25.1% versus 11.0% of cryptococcal meningitis [27,28]. A study done by Wadia et al showed cryptococcal meningitis was more common than tubercular meningitis. This difference in the prevalence of tuberculosis and cryptocoocus meningitis is due to the different distribution of tuberculosis in different parts of India. Tuberculosis is the commonest neurological disorder in this study presenting as both opportunistic infection and co-infection with HIV. Its risk increases 15 times-30 times in HIV infection. According to NACO, tuberculosis is the most commonly occurring infection in HIV both pulmonary and extrapulmonary The mean CD4 count was high for TB in our study which is similar to western data. CD4 count is directly proportional to neurological symptoms in HIV-positive patients. With lowering of CD4 count accounts for more neurological disorders in HIV patients. Studies have also reported the presence of neurological complications as well as other clinical manifestations associated with decreased CD4 count and increased viral load. 20 patients had CD4 count between 200/mm³ to 500/mm³, out of which, 14 were of Tubercular Meningitis (TBM), 2 of Pyogenic Meningitis(PM), and 1 of fungal meningitis, and 2 were undiagnosed. This correlates with the study of Crowe S M et al. which showed that tuberculosis and oropharyngeal candidiasis develop when CD4 count is in the range of 250/mm³-500/mm³ [29]. When the CD4 count decline to approximately 100/mm³, common AIDS-defining opportunistic infections develop, such as toxoplasmosis, cryptococcal meningitis, etc. Similar to our findings, a study from the USA also stated that tuberculosis meningitis can occur at any CD4 count level, while cryptococcal meningitis usually occurs when the CD4 count is less than 200 [30].

HIV-associated dementia occurred in 4 cases of this study which is similar to studies done by Wadia et al10 and Deshpande et al who reported 4.35 and 5% cases respectively. Studies from western countries reported 20%-30% of cases, mostly in advanced HIV infection [31,32].

The present study reported 16 cases (15.84%) of oral candidiasis associated with other neurological manifestations, while in other studies, oral candidiasis has been described as the second most common opportunistic infection [33,34]

15 cases (14.85%) had viral encephalitis in the present study. It occurs in 15%-40% of cases of HIV, though no systemic studies are available 5 patients with viral encephalitis were not on treatment and 2 patients were taking interrupted treatment [35].

Out of 32 cases (31.68%) of TBM 15 cases (14.85%) had only TBM while the following percentage of patients had additional Opportunistic infection:

- 5 cases (4.9%) were associated with oral candidiasis.
- 4 cases (3.9%) with HBV infection.
- 1 case(0.99%) with meningoencephalitis.
- 1 case of tubercular meningitis with cryptococcal meningitis.
- 1 case of tubercular meningitis with HIV-associated dementia was seen.

11 patients with TBM were not taking treatment and 2 patients were taking interrupted treatment.5 patients out of 32 had disseminated TB.

Cryptococcal meningitis was seen in 14 cases (13.88%) with 7 cases (6.93%) having isolated *Cryptococcus meningitis* and the remaining patients had additional opportunistic infection:

- 5 cases (4.9%) with oral candidiasis.
- 1 case (0.99%) with hydrocephalus.
- 1 case (0.99%) with TBM.

7 patients with *cryptococcal meningitis* were not on treatment and 5 patients were taking interrupted treatment.

CONCLUSION

In conclusion, this study emphasizes the fact that tuberculosis and cryptococcus infections are the frequent opportunistic infections associated with HIV. There is a direct correlation between CD4 count and severity of infection, hence indicating the level of immunity and disease. It also shows that various neurological manifestations are due to these opportunistic infections. This dual course of HIV and opportunistic infections should be controlled by providing awareness of the disease transmission, progression, and prevention. Due to the high cost of Highly Active Anti-Retroviral Drugs (HAART) and the low availability of HIV centers, patients lack access to proper treatment which in turn leads to the development of opportunistic infections in the later course of the disease. CD4 counts are important in managing specific therapy for HIV-positive patients.

FUNDING

None.

CONFLICT OF INTEREST

None.

REFERENCES

1. Sepkowitz KA. AIDS—the first 20 years. New England Journal of Medicine. 2001;344(23):1764-72.
2. Global HIV & AIDS statistics- 2020 fact sheet [Internet]. Unaids.org. [cited 2021 Feb 7]. Available from:https://www.unaids.org/en/resources/fact-sheet.
3. UNAIDS, WHO 2011, Global Report, UNAIDS Report on the Global epidemic, 2011.
4. Knoll B, Lassmann B, Temesgen Z. Current status of HIV infection: a review for non-HIV-treating physicians. International journal of dermatology. 2007; 46(12):1219-28.
5. Fauci AS. Human immunodeficiency virus disease: AIDS and related disease. Harrison's Internal Medicine. 2008:1137-204.cUNAIDS, WHO Dec 2007, AIDS epidemic update, 2007.
6. Smith, Blaine T. Concepts in immunology and immunotherapeutic. 4th ed American society of health system pharmacist, 2008;143.
7. Cheung MC, Pantanowitz L, Dezube BJ. AIDS-related malignancies: emerging challenges in the era of highly active antiretroviral therapy. The oncologist. 2005; 10(6):412-26.WHO 2012, Tuberculosis, Fact sheet 104, March 2012.
8. Wadia RS, Pujari SN, Kothari S, et al. Neurological manifestations of HIV disease. J Assoc Physicians India. 2001 Mar;49:343-8.
9. Weinberg JL, Kovarik CL. The WHO clinical staging system for HIV/AIDS. AMA Journal of Ethics. 2010 ;12(3):202-6.
10. Park's K. Park's text book of preventive and social medicine.
11. Singh R, Kaur M, Arora D. Neurological complications in late-stage hospitalized patients with HIV disease. Annals of Indian Academy of Neurology. 2011 ;14(3):172.
12. Ramesh K, Gandhi S, Rao V. Clinical profile of human immunodeficiency virus patients with opportunistic infections: A descriptive case series study. International Journal of Applied and Basic Medical Research. 2015;5(2):119.
13. Boruah PK, Adhikari AK. Clinical spectrum of HIV/AIDS presenting to Gauhati Medical College. J Assoc Physicians India. 2003;51:1258-60.
14. Korzeniewska-Kosela M, Fitz Gerald JM, Vedal S, Allen EA, Schechter MT, Lawson L, Phillips P, Black W, Montaner JS. Spectrum of tuberculosis in patients with HIV infection in British Columbia: report of 40 cases. CMAJ: Canadian Medical Association Journal. 1992 ;146(11):1927.
15. Sharma SK, Kadhiravan T, Banga A, Goyal T, Bhatia I, Saha PK. Spectrum of clinical disease in a series of 135 hospitalised HIV-infected patients from north India. BMC infectious Diseases. 2004;4(1):1-9.
16. Vajpayee M, Kanswal S, Seth P, Wig N. Spectrum of opportunistic infections and profile of CD4+ counts among AIDS patients in North India. Infection. 2003 ;31(5):336-40.
17. Goud TG, Ramesh K. Opportunistic infections among HIV patients attending Tertiary care hospital, Karnataka, India. International Journal of current microbiology and applied sciences. 2014;3(4):824-9.
18. Giri TK, Pande I, Mishra NM, Kailash S, Uppal SS, Kumar AS. Spectrum of clinical and laboratory characteristics of HIV infection in northern India. The Journal of Communicable Diseases. 1995 Sep 1;27(3):131-41.
19. Singh A, Bairy I, ShivanandaPG. Spectrum of opportunistic infection in AIDS cases. Indian J Med Sci. 2003;57:16-21.
20. Bolokadze N, Gabunia P, Ezugbaia M, et al. Neurological complications in patients with HIV AIDS. Georgian Med News.2008;1(165):34-8.
21. Brew BJ, Miller J. Human immunodeficiency related virus-related headache. Neurology. 1993;43(6):1098-100.
22. Sonkar SK, Gupta A, Atam V, et al. Clinical Profile of Neurological Manifestation in Human Immunodeficiency Virus-positive Patients. N Am J Med Sci. 2012;4(11):596-9.
23. Pal J, Karmakar PS, Ray A, et al. Opportunistic infections of central nervous system in AIDS. J Indian Med Assoc. 2009;107(7):446-9.
24. Holtzman DM, Kaku DA, So YT. New onset seizure associated with Human immunodeficiency virus infection: causation and clinical features in 100 cases. Am J Med. 1989;87(2):173-7.
25. Teja VD, Talasila SR, Vemu L. Neurologic manifestations of HIV infection: an Indian hospital-based study. AIDS Read. 2005;15(3):139-43.
26. Attili SVS, Gulati AK, Singh VP, et al. Diarrhea, CD4 counts and enteric infections in a hospital - based cohort of HIV-infected patients around Varanasi, India. BMC Infect Dis. 2006;6(1):1-8.
27. Crowe SM, Carlin JB, Stewart KI, et al. Predictive value of CD4 lymphocyte numbers for the development of opportunistic infections and malignancies in HIV-infected persons. J acquir immune defic syndr. 1991;4(8):770-6.
28. Vinnard C, Macgregor RR. Tuberculous meningitis in HIV-infected individuals. Curr HIV/AIDS Rep. 2009;6(3):139-45.
29. Deshpande AK, Patnaik MM. Nonopportunistic neurologic manifestations of the human immunodeficiency virus: an Indian study. Journal of the International AIDS Society. 2005;7(1):2.
30. Navia BA, Jordan BD, Price RW. The AIDS dementia complex: I. Clinical features. Annals of Neurology: Official Journal of the American Neurological Association and the Child Neurology Society. 1986;19(6):517-24.
31. Sharma SK, Kadhiravan T, Banga A, et al. Spectrum of clinical disease in a series of 135 hospitalised HIV-infected patients from north India. BMC infectious Diseases. 2004;4(1):1-9.
32. Saag MS, Graybill RJ, Larsen RA, et al. Practice guidelines for the management of cryptococcal disease. Clinical Infectious Diseases. 2000 Apr 1;30(4):710-8.
33. Shankar SK, Mahadevan A, Satishchandra P, et al. Neuropathology of HIV/AIDS with an overview of the Indian scene. Indian Journal of Medical Research. 2005;121:468-88.