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Original Research Article

Study of Cerebro-Spinal Fluid in HIV Infected Patients at a Tertiary Care Hospital in Maharashtra

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Abstract:

Background: The incidence of neurological complications directly related to human immunodeficiency virus (HIV) infection has not decreased proportionally, probably due to low penetration of anti-retroviral (ARV) drugs into the central nervous system (CNS), the neuronal toxicity of ARVs or the persistence of neuronal lesions caused by HIV infection before treatment. Hence, cerebrospinal fluid (CSF) analysis will be used clinically to treat opportunistic infections and co-infections.

Method: 80 (eighty) adult HIV infected patients after 4-6 weeks of diagnosis aged between 19-50 years were studied. HIV infection was confirmed by retesting at our centre. Also, CD4 cell count was done. CSF was drained through a lumbar puncture under all aseptic precautions with standard protocols. MRI Brain was also done to rule out brain tumours and brain atrophy.

Results: In the CD4 cell count study, 48 (60%) had 83 to 100 cells/mm³, and 32 (40%) had 101–140 cells/mm³. 25 (31.2%) HIV infected patients had Tuberculosis (TB), 41 (51.2%) had Candidiasis, 11 (13.7%) had Diarrhoea and 3 (3.75%) had Pneumonia as associated co-morbidities. The CSF analysis findings were: Proteins- 52 (65%) patients had 75-80 mg/dl, 28 (35%) had 81-90 mg/dl, Glucose- 50 (62.5%) had 38.44 mg/dl, 30 (37.5%) had 45-50 mg/dl, Cell count- 46 (57.5%) had 5-7/µL, 34 (42.5%) had 8-10/µL. India ink staining: 34 (42.5%) had 19-25 Cryptococci and 46 (57.5%) had 20–26 Cryptococci per high power field (hpf), Cryptococcal Antigen titre: 25 (31.2%) had 1:16, 55 (68.7%) had 1:32. The Cryptococcal culture (base line) was: 60 (75.1%) had 20–26 colony forming units (CFU)/ml, and 20 (25%) had 27–29 CFU/ml.

Conclusion: CSF analysis has a well-defined and valuable role in the diagnosis of CNS infections in HIV/AIDS patients. It will help the clinician treat and avoid morbidity and early mortality because HIV infection is treatable, not curable.

Keywords: HIV/AIDS, Cerebrospinal fluid, CD4 cell count, lumbar puncture, Tuberculosis.

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Introduction

The Central Nervous System (CNS) and Immune System are HIV target organs. The introduction of highly active anti-retroviral therapy (HAART) has changed the clinical situation for patients with acquired immunodeficiency syndrome (AIDS), decreased the incidence of opportunistic infections, and thus lowered mortality [1]. However, the incidence of neurological complications directly related to HIV infection has not decreased proportionally, probably because of the low penetration of anti-retroviral (ARV) drugs into the CNS, the neuronal toxicity of ARVs or the persistence of neuronal lesions caused by HIV infection before treatment [2].

In the clinical practice, CSF analysis in HIV infected patients is indicated for the diagnosis of opportunistic infections and co-infections, the diagnosis of meningitis (acute or chronic) caused by HIV, and the quantification of HIV viral load in the CNS [3]. Acute meningitis affects 5–10% of HIV infected patients [4]. The CSF has biochemical and cellular patterns that reflect the diseases of the brain and spinal cord. Hence, patients at the risk of HIV infection are advised to have serological and other diagnostic tests for HIV after 4-6 weeks. No specific biomarker in the CSF or blood helps to diagnose acute meningitis caused by HIV.

Chronic meningitis affects 40% of the infected individuals and 59% are symptomatic. Hence, CSF analysis is mandatory for HIV infected patients because CSF presents with pleocytosis (5–50 cells/µL) and an increased total proteins level (50–100 mg/dl). Hence, an attempt is made to evaluate the CSF in chronic HIV infected patients.

Material and Method: 80 (eighty) HIV infected patients referred to the pathology department of ACPM Medical College and Hospital Dhule, Maharashtra, were studied.

Inclusive Criteria: Patients aged between 19-50 years with symptoms of HIV infection associated with diarrhoea, candidiasis, tuberculosis and a decreased CD4 cell count were selected for the study.

Exclusion Criteria: Patients with malignancy, septicaemia, and cardio-vascular diseases were excluded from the study.

Method: The HIV test was done again along with the CD4 cell count to confirm the diagnosis of admitted patients.

Neurological symptoms like headache, mental confusion, dizziness, vomiting, and seizures were noted and CSF was drained through a lumbar puncture for detailed analysis. In most of the cases, the CSF was gelatinous or fibrous. MRI of the brain was also done to rule out any brain tumour or brain atrophy.

The duration of the study was from July 2022 to June 2023.

Statistical analysis: Clinical manifestations, baseline study-associated diseases, and contents of CSF were classified by percentage. The statistical study was carried out using SPSS software.

Observation and Results

Table 1: Study of baseline parameters in HIV infected patients

- Body weight: 49 (61.2%) had 38 to 45 kg, and 31 (38.7%) had 46–56 kg.
- Serum creatinine: 44 (55%) had 0.80 to 0.90 mg/dl, and 36 (45%) had 0.91 to 1.0 mg/dl.
- CD4 cell count: 48 (60%) had 83 to 100 cells/mm³, and 32 (40%) had 101 to 140 cells/mm³.

Table 2: Clinical manifestations of HIV infected patients: 32 (40%) had headache, 9 (11.2%) had fever, 14 (17.5%) had mental confusion, 13 (16.2%) had vomiting, 7 (8.75%) had dizziness, and 5 (6.25%) had seizures.

Table 3: Study of associated morbidities in HIV infected patients: 25 (31.2%) had Tuberculosis, 41 (51.2%) had Candidiasis, 11 (13.7%) had Diarrhoea, and 3 (3.75%) had Pneumonia.

Table 4: Study of the contents of CSF in HIV infected patients

- Proteins: 52 (65%) had 75–80 mg/dl, and 28 (35%) had 81–90 mg/dl.
- Glucose: 50 (62.5%) had 38–44 mg/dl, and 30 (37.5%) had 45–50 mg/dl.
- Cell count: 46 (57.5%) had 5-7/µL, 34 (42.5%) 8-10/µL.
- India Ink Staining: 34 (42.5%) had 19–25 Cryptococci per hpf, 46 (57.5%) had 20–26 Cryptococci per hpf.
- Cryptococcal Antigen titre: 25 (31.2%) had 1:16, 55 (75%) had 1:32.
- Cryptococcal culture (base line): 60 (75%) had 20–26 CFU/ml, and 20 (25%) had 27–29 CFU/ml.

Table 1: Study of base line parameters in HIV infected patients (No. of patients: 80)

Sl. No	Parameters	No. patients	Percentage
1	Body weight 38-45 kg 46-56 kg	 49 31	 61.2 38.7
2	Serum creatinine 0.80 to 0.90 mg/dl 0.91 to 1.00 mg/dl	 44 36	 55 45
3	CD4 cell count 83 to 100 cells/mm^3 101 to 140 cells/mm^3	 48 32	 60 40

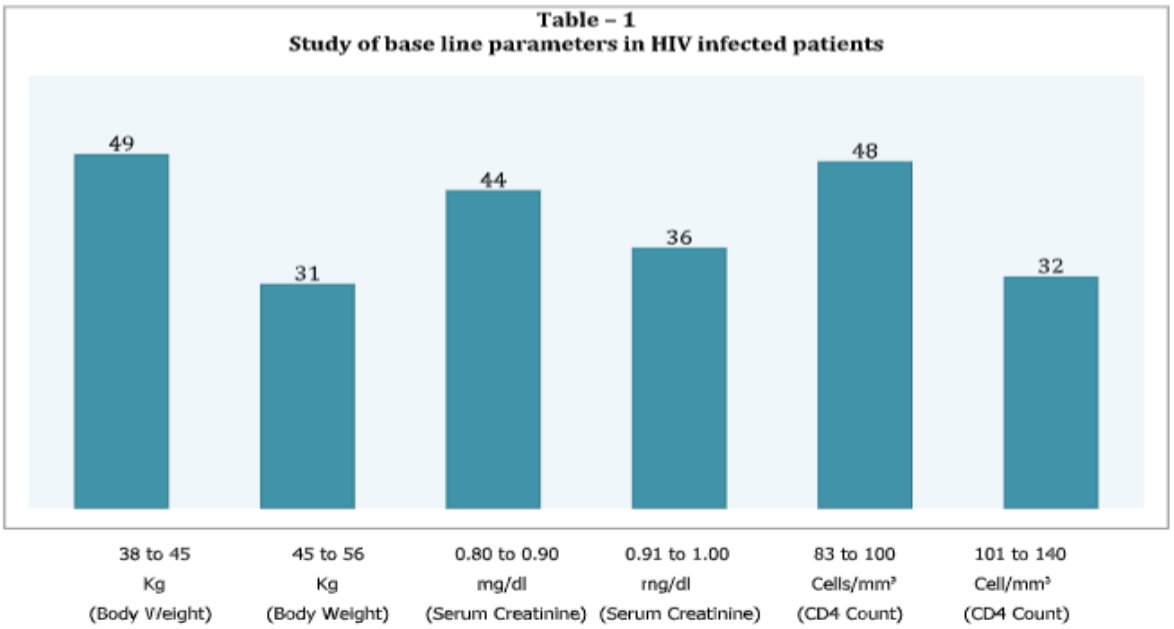

Figure 1: Study of base line parameters in HIV infected patients

Table 2: Clinical manifestations in HIV infected patients

Sl. No	Particulars	No. of patients (80)	Percentage
1	Headache	32	40
2	Fever	9	11.2
3	Mental confusion	14	17.5
4	Vomiting	13	16.2
5	Dizziness	7	8.75
6	Seizures	5	6.25

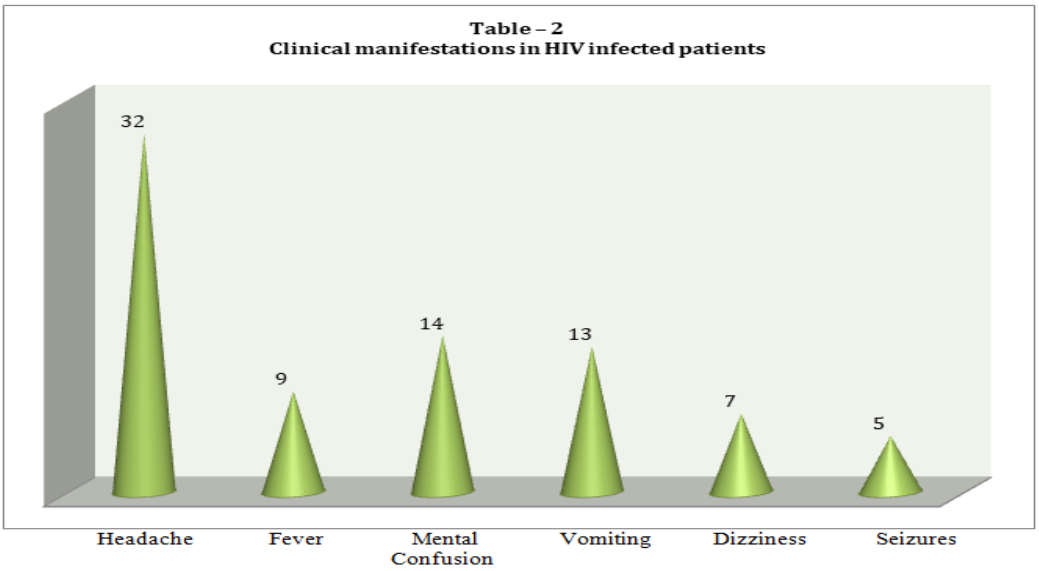

Figure 2: Clinical manifestations in HIV infected patients

Table 3: Study of associated diseases in HIV infected patients

Sl. No	Diseases	No. of patients (80)	Percentage
1	Tuberculosis (TB)	25	31.2
2	Candidiasis	41	51.2
3	Diarrhoea	11	13.7
4	Pneumonia	03	3.75

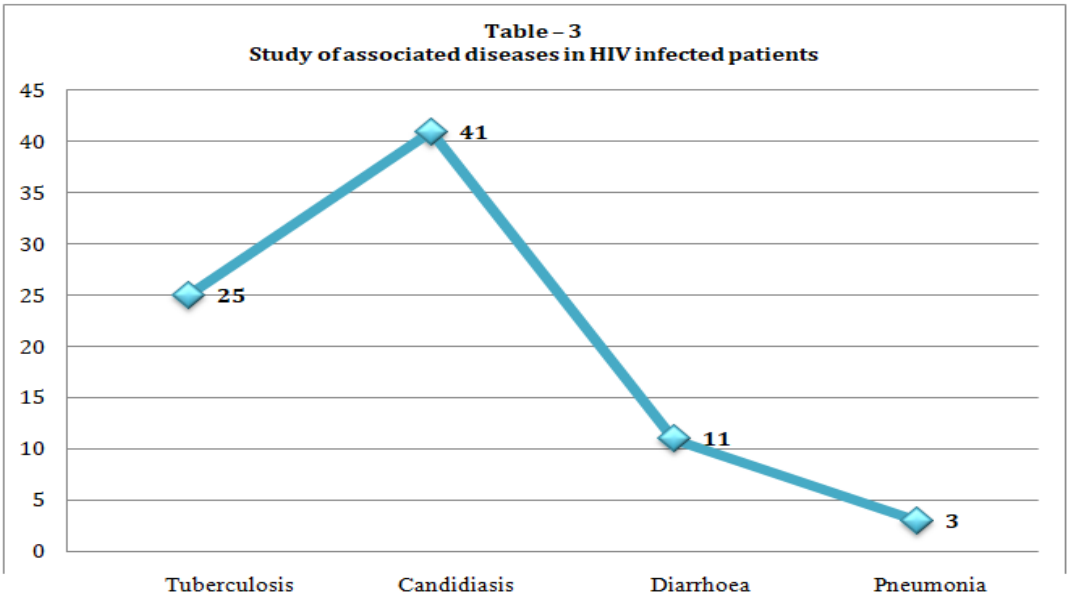

Figure 3: Study of associated diseases in HIV infected patients

Table 4: Study of the Contents of CSF in HIV infected patients

Sl. No	Contents	No. of patients (80)	Percentage
1	Proteins 75-80 mg/dl 81-90 mg/dl	 52 28	 65 35
2	Glucose 38-44 mg/dl 45-50 mg/dl	 50 30	 62.5 37.5
3	Cells 5-7/µL 8-10/µL	 46 34	 57.5 42.5
4	India Ink staining 19-25 cryptococci/hpf 20-26 cryptococci/hpf	 34 46	 42.5 57.5
5	Cryptococcal antigen titre 1:16 1:32	 25 55	 31.2 68.7
6	Cryptococcal culture (base line) 20-26 CFU/ml 27-29 CFU/ml	 60 20	 75 25

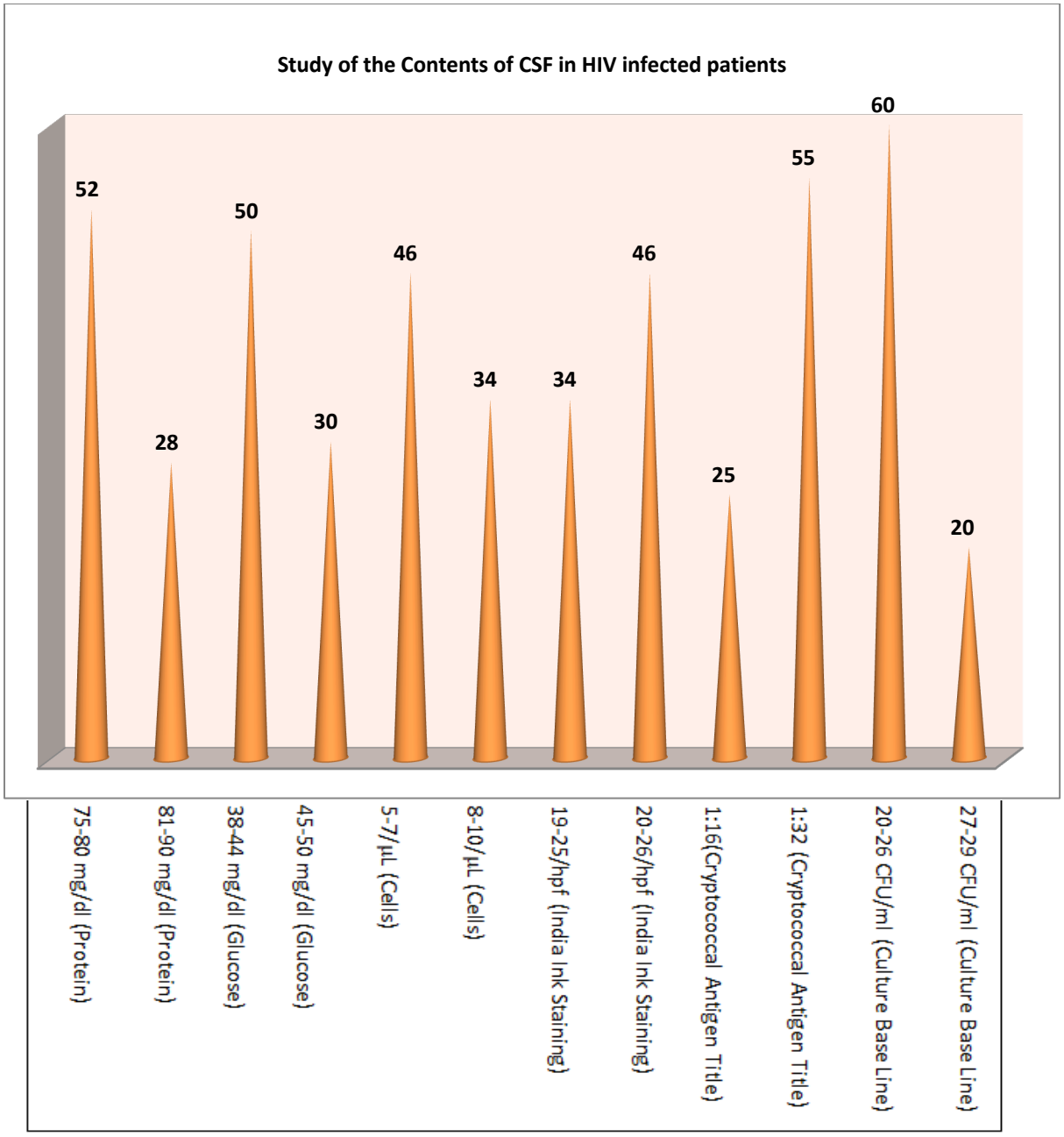

Figure 4: Study of the Contents of CSF in HIV infected patients

Discussion

In the present study of CSF in HIV infected patients at a tertiary care hospital in Maharashtra, body weight in 49 (61.2%) patients was 38–45 kg, and in 31 (38.7%) patients, it was 46–56 kg. In the serum creatinine study, 44 (55%) had 0.80 to 0.90 mg/dl and 36 (45%) had 0.91 to 1.00 mg/dl. CD4 cell count in 48 (60%) patients was 83 to 100 cells/mm3 and in 38 (40%) patients it was 101 to 140 cells/mm3 (Table 1). The clinical manifestations of HIV patients were: 32 (40%) had headache, 9 (11.2%) had fever, 14 (17.5%) had mental confusion, 13 (16.2%) had vomiting, 87 (8.75%) had dizziness and 5 (6.25%) had seizures (Table 2). The study of associated diseases found that 25 (31.2%) had tuberculosis, 41 (51.2%) had Candidiasis, 11 (13.7%) had diarrhoea, and 3 (3.75%) had pneumonia (Table 3). In the study of the contents of CSF, 52 (65%) patients had 75–80 mg/dl and 28 (35%) had 81–90 mg/dl of proteins in their CSF.

In glucose analysis, 50 (62.5%) had 38–44 mg/dl, and 30 (37.5%) had 45–50 mg/dl. Also, cell counts showed that 46 (57.5%) had 5-7 cells/µL and 34 (42.5%) had 8-10 cells/µL. In India ink staining, 34 (42.5%) had 19–25 Cryptococci per hpf, 46 (57.5%) had 20–26 Cryptococci per hpf. In Cryptococcal antigen titre, 25 (31.2%) had 1:16, 55 (68.7%) had 1:32 titre. In Cryptococcal culture (base line), 60 (75%) had 20–26 CFU/ml, and 20 (25%) had 27–29 CFU/ml (Table 4). These findings are more or less in the agreement with previous studies [5,6,7].

The use of CSF analysis for the specific diagnosis of HIV-associated neurocognitive disorders (HAND), HIV myelopathy, and immune reconstitution inflammatory syndrome (IRIS-HIV) has clinical importance, but specific biomarkers for the diagnosis of these diseases have not been identified.

HAND is the main neurological complication directly associated with HIV infection. It is a clinical diagnosis. [8] CSF analysis is important for ruling out opportunistic infections and co-infections. Several biomarkers to study CSF with potential have been studied, but they are not clinically applicable and are used only in the research studies [9]. Neurons do not have CD4 receptors. HIV does not infect neurons, but affect them indirectly, due to the complex interactions of inflammatory and neuronal injury proteins and also the fact that HIV proteins cause injury to neurons.

The CNS and Immune systems are the HIV-target organs. However, the incidence of neurological complications related to the HIV infection has increased considerably [10] probably because of the low penetration of anti-retroviral (ARV) drugs into the CNS, the neuronal toxicity of ARV drugs or the persistence of neuronal lesions that might have been caused before treatment [11]. It is also reported that polyneuropathies are associated with HIV infection. The cells observed in CSF are apoptotic, which are dead due to infection caused by HIV. It is also noted that different concentrations of ARV drugs are found in the CSF that penetrate the blood-brain barrier (BBB), which is considered necessary to control infection in the CNS in patients at an advanced stage of the disease, particularly those with neurological problems [12]. Cryptococcal meningitis is one of the acquired immune deficiency syndrome defining infections with high morality because of the low penetration of ARV drugs.

Summary and Conclusion

The present study of CSF analysis has a well-defined and valuable role in the diagnosis of opportunistic infections and co-infections in HIV/AIDS patients. But this study demands further research to establish a clinically applicable biomarker for the diagnosis of HIV-associated neuro-cognitive disorders, including promising CSF biomarkers including neopterin and neurofilament light chain (NFL), because the exact biomarker in the CSF to diagnose HIV/AIDS has yet to be identified.

Limitation of Study: Owing to the tier-3 city location of the research centre, the small number of patients, and the lack of the latest technologies, we have limited findings and results.

This research paper has been approved by the ethical committee of ACPM Medical College and Hospital, Dhule, Maharashtra (424001).

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