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Article

Neurological Disorders Associated with Human Immunodeficiency Virus - acquired immunodeficiency syndrome in Patients Diagnosed with Human Immunodeficiency Virus at a Tertiary Care Hospital in Quetta

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ABSTRACT

Background: Neurological complications in HIV/AIDS are a significant but underreported public health concern in Pakistan, especially in underserved regions like Balochistan. Despite known global prevalence, regional data are lacking, creating a gap in targeted interventions and care planning. **Objective**: To determine the frequency and distribution of neurological manifestations among HIV-positive patients admitted to a tertiary care hospital in Quetta, with an emphasis on demographic, clinical, and radiological correlations. **Methods**: This descriptive cross-sectional study was conducted at the Department of Neurosurgery, Bolan Medical College Hospital (BMCH), Quetta, from January 1 to December 31, 2024. A total of 177 HIV-positive patients aged >20 years presenting with clinical evidence of nervous system involvement were enrolled. Data were collected through standardized history, neurological examination, laboratory investigations, and neuroimaging. Ethical approval was obtained per the Helsinki Declaration. Data analysis was performed using SPSS v26, employing descriptive statistics and chi-square tests for post-stratification associations. **Results**: Tuberculous meningitis was the most common manifestation (56.5%), followed by dementia (17.5%), myelopathy (10.2%), peripheral neuropathy (9.6%), and AIDS-related stroke (6.2%). Neurological involvement was higher in males (68.4%) and those from lower socioeconomic backgrounds (54.2%). **Conclusion**: HIV/AIDS exerts a significant neurological burden, especially in resource-limited regions. Early identification and management of neuro-HIV complications can improve quality of life and reduce mortality.

Keywords: HIV Infections, AIDS, Neurologic Manifestations, Tuberculous Meningitis, Peripheral Neuropathy, HIV Dementia, Resource-Limited Settings

INTRODUCTION

The Human Immunodeficiency Virus (HIV) is a pathogen that targets the cells of the immune system, rendering the body susceptible to opportunistic infections (1). Additionally, HIV infection can result in neurological complications, as the virus is classified among lentiviruses, which are associated with a heightened risk of chronic neurological diseases in human hosts (2). The nervous system is one of the most frequently and severely affected systems in individuals with HIV infection, with 40% to 70% of infected individuals developing symptomatic neurological disorders (3). Although nervous system involvement typically occurs in conjunction with profound immunosuppression and other acquired immunodeficiency syndrome (AIDS)-defining illnesses, it can precede AIDS in 10% to 20% of HIV seropositive individuals (4). The classification of HIV-related neurological diagnoses has recently been revised and updated. The neurological complications of AIDS, collectively referred to as Neuro AIDS, encompass neurocognitive impairment and HIV-associated dementia (HAD; also known as AIDS dementia and HIV encephalopathy) (5). HAD represents the most significant and debilitating central nervous system (CNS) complication associated with HIV infection. Patients with less severe afflictions exhibit a milder form of impairment known as HIV-associated minor cognitive/motor disorder (MCMD) (6). A study conducted by Telles JP in Brazil highlighted the

neurological manifestations of HIV-AIDS, reporting cerebral toxoplasmosis (36%), cryptococcal meningitis (14%), and tuberculous meningitis (8%) as prevalent manifestations among HIV-AIDS patients (7).

This research provides valuable insights into the prevalence and distribution of neurological manifestations across different stages of HIV infection. It is also crucial for healthcare providers and policymakers, as it informs public health strategies, resource allocation, and the development of comprehensive care plans for individuals with HIV-AIDS. In summary, investigating the frequency of neurological manifestations in HIV-AIDS patients is essential for advancing the understanding of the disease's impact on the nervous system and is vital for optimizing clinical management and enhancing the overall well-being of affected individuals.

MATERIAL AND METHODS

This descriptive study was conducted in the Department of Neurology/Neurosurgery at Bolan Medical College/Hospital Quetta. Following approval from the ethical review committee, the sample size was calculated using the WHO sample size calculator, with a confidence level (1-α) of 95%, a desired precision (d) of 4%, and an estimated population frequency of tuberculous meningitis as a neurological manifestation of HIV-AIDS at 8%, as derived from the parent study.(7) The largest calculated sample size was 177. All inpatients from the ward or emergency room with HIV-AIDS were enrolled in the study and underwent comprehensive history-taking and physical examinations. Informed consent was obtained from each participant. Demographic information, including patient ID number, sex, weight (measured using a Camry analogue weighing scale), and height (measured with a stadiometer), was recorded in a proforma. The researchers, all infectious disease specialists, were trained by a team of neurologists to minimize heterogeneity in neurological examinations. Patients were included in the study between 24 and 48 hours after hospital admission. Standardized forms were used to document demographic, clinical, laboratory, and radiological details. Following inclusion, polymerase chain reaction (PCR), cultures, and serology/antigen results from blood and cerebrospinal fluid (CSF) were analyzed. Computed tomography (CT), magnetic resonance imaging (MRI), nerve conduction velocity (NCV), and single-photon emission computed tomography were available for patient diagnosis if necessary. Infectious disease specialists, following routine institutional protocols, were responsible for diagnosis and treatment decisions, with specialists in neuroradiology, neurology, and neurosurgery available as needed. Pre- and post-discharge CD4+ lymphocyte cell counts, HIV viral loads, and combination antiretroviral therapy (cART) regimens were obtained. Exclusion criteria were rigorously applied to control for effect modifiers and bias in the study results. A database was developed using SPSS for Windows version 26.0. Mean values and standard deviations were calculated for quantitative variables such as age, weight, body mass index (BMI), and duration of illness. The normality of the data was assessed using the Shapiro-Wilk test. Frequencies and percentages were presented for qualitative variables such as gender (male/female), place of residence (urban/rural), neurological manifestations (dementia, tuberculous meningitis, myelopathy, peripheral neuropathy/stroke), and socioeconomic status (upper/middle/lower). Effect modifiers were controlled through stratification by age, gender, and place of residence to assess their impact on outcome variables. Post-stratification, the chi-square test or Fisher's exact test (if frequency ≤5 in any cell) was applied. P-values of ≤0.05 were considered statistically significant.

RESULTS

The most prevalent condition observed in the duration of illness was tuberculosis meningitis, accounting for 100 cases (57%). This was followed by dementia, with 31 cases (18%), and myelopathy, with 18 cases (10%). Additionally, 17 patients (10%) were diagnosed with peripheral neuropathy, and 11 patients (6%) experienced AIDS-related stroke. Table no. 1 provides further details.

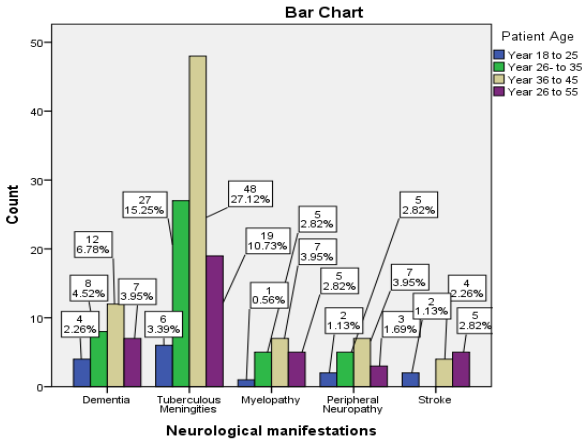

Figure No. 1 Neurological manifestations * Patient Gender

The statistical analysis of patient outcomes revealed a mean age of 2.7966 with a standard deviation of 0.88124. The mean gender value of the total patient cohort was 1.3164, with a standard deviation of 0.46638, and the age range was 3.

Table No. 1 Frequency to Age, Gender, Place of Residence Socioeconomic Status Duration of Illness and Neurological Manifestations

	Study Variables	Frequency	Percent (%)
Age Group	20 to 25 Years	15	8.5
	26- to 35 Years	45	25.4
	36 to 45 Years	78	44.1
	26 to 55 Years	39	22.0
Gender	Male	121	68.4
	Female	56	31.6
Place of Residence	Urban	89	50.3
	Rural	88	49.7

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	Study Variables	Frequency	Percent (%)
Socioeconomic Status	High	19	10.7
	Middle	62	35.0
	Low	96	54.2
Duration of Illness (in Months)	1	34	19.2
	2	27	15.3
	3	39	22.0
	4	23	13.0
	5	19	10.7
	6	22	12.4
	7	4	2.3
	8	9	5.1
Weight (in KG)	<5%	21	11.9
	Between 5% and 10%	55	31.1
	>10%	101	57.1
Body Mass index	18.5	22	12.4
	17 to 18.4	47	26.6
	16 to 16.9	25	14.1
	< 16	83	46.9
Neurological Manifestations	Dementia	31	17.5
	Tuberculous Meningitis	100	56.5
	Myelopathy	18	10.2
	Peripheral Neuropathy	17	9.6
	Stroke	11	6.2
	Total	177	100.0

Table No. 2 Statistics of Age, Gender, Place of Residence Socioeconomic Status Duration of Illness and Neurological Manifestations

	Patient Age	Patient Gender	Place of Residence	Socioeconomic Status	Duration of Illness (in Months)	Neurological manifestations
Mean	2.7966	1.3164	1.4972	2.4350	3.53	2.3051
Std. Deviation	.88124	.46638	.50141	.68050	1.995	1.06474
Range	3.00	1.00	1.00	2.00	7	4.00

Table No 3 Neurological Manifestations compared with Patients Gender * Place of Residence

Neurological manifestations			Place of Residence		Total
			Urban	Rural	
Dementia	Patient Gender	Male	10	11	21
		Female	4	6	10
	Total		14	17	31
Tuberculosis Meningitis	Patient Gender	Male	29	43	72
		Female	16	12	28
	Total		45	55	100
Myelopathy	Patient Gender	Male	4	7	11
		Female	6	1	7
	Total		10	8	18
Peripheral Neuropathy	Patient Gender	Male	3	4	7
		Female	7	3	10
	Total		10	7	17
Stroke	Patient Gender	Male	9	1	10
		Female	1	0	1
	Total		10	1	11
Total	Patient Gender	Male	55	66	121
		Female	34	22	56
	Total		89	88	177

The mean value for neurological manifestations was 2.3051, with a standard deviation of 1.0647 and a range of 4. Table no. 2 presents these findings. Post-satisfaction analysis is illustrated in Table no. 3 and Figure no. 1.

DISCUSSION

The involvement of the nervous system in patients with human immunodeficiency virus-acquired immunodeficiency syndrome (HIV-AIDS) is well-documented, with no part of the neuraxis remaining unaffected by the virus.(5) Neurological symptoms in HIV patients may result from the primary pathological effects of

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the HIV infection itself or from opportunistic infections or neoplasms.(6) The infiltration of infected macrophages into the brain parenchyma leads to progressive neurodegeneration, particularly affecting the hippocampus, basal ganglia, prefrontal cortex, and white matter. Damage to the central nervous system may occur due to the release of neurotoxins and cytokines, including IL-1, TNF, and IL-6.(7)

To date, no research has been conducted on the neurological manifestations associated with AIDS in Balochistan. In the present study, the incidence of neurological involvement was observed to be lowest and highest within the age range of 18 to 55 years, consistent with findings from other studies. This age group represents a crucial segment of society, with potential implications for national development and the well-being of future generations.(1) The study revealed that the disease was primarily transmitted through heterosexual interactions, with the presence of multiple partners and engagement with commercial sex workers contributing to this mode of transmission. This finding contrasts with research conducted in Western regions, where homosexual transmission is more prevalent. (8)

The most common neurological complication of HIV infection aligns with findings from other studies, such as those from the Nizam Institute of Medical Sciences (NIMS), where the incidence of tuberculous involvement was 25% and 26%, respectively.(9,10) Neurological manifestations represent the most prevalent fungal infection among patients infected with HIV. In the United States, it is estimated that approximately 5–10% of individuals with AIDS are affected by cryptococcal meningitis. In this research, 13 out of 91 (14.2%) patients diagnosed with neuro-AIDS were found to have cryptococcal meningitis. The primary symptoms reported included fever, headache, and vomiting, accompanied by altered mental status. The pathogen responsible, Cryptococcus neoformans, induces minimal inflammatory response in AIDS patients with compromised immune systems, accounting for the rarity of neck stiffness and photophobia in these findings. Cryptococcal meningitis typically manifests in the advanced stages of HIV infection, particularly when CD4 counts fall below 100 µl.(11)

The analysis of cerebrospinal fluid (CSF) in patients with cryptococcal meningitis indicated average protein levels of 120 mg, glucose levels of 67 mg, a total cell count of 40 cells/mm^3, and lymphocyte percentages of 92%. In this study, the CSF cryptococcal antigen titer was identified as the gold standard for diagnostic evaluation. Similar findings have been reported in other research studies.(11,12) A heightened level of suspicion is essential for the accurate diagnosis of cryptococcal meningitis. In patients with HIV infection, the mortality rate following the onset of cryptococcal meningitis was observed to be 40%. Key negative prognostic indicators included altered mental status at the time of diagnosis, positive India ink staining, a low leukocyte count in CSF, positive blood cultures, elevated cryptococcal antigen levels, hypoglycorrhachia in CSF, and increased opening pressure of the CSF. Other secondary central nervous system conditions that presented similarly included cryptococcal meningitis, toxoplasmosis, progressive multifocal leukoencephalopathy (PML), and neurosyphilis, aligning with the findings from the NIMS study.(9,10,11,12) In a Brazilian study, toxoplasmosis was the most common cause of secondary CNS manifestation.(12,13,14) The most prevalent manifestation of toxoplasmosis was the emergence of new-onset seizures, followed by focal neurological deficits. The most sensitive diagnostic method for this condition is MRI with contrast. This infection typically occurs in individuals with a CD4 count below 100 cells per cubic millimeter.(7) Progressive multifocal leukoencephalopathy results from infection with the human polyoma virus (JC virus), developing in 4% of patients with AIDS, and this was the initial manifestation of AIDS in 29% of these cases.(5) In the context of the AIDS epidemic, there has been a significant increase in syphilis cases, along with a notable rise in the occurrence of neurosyphilis. This correlation is not surprising, as both AIDS and neurosyphilis are transmitted through sexual contact. It is noteworthy that neurosyphilis has been observed to manifest in approximately one-third of individuals who advance to the later stages of the disease.(15)

HIV-related neurocognitive impairment, myelopathy, peripheral neuropathy, myopathy, and aseptic meningitis represent the primary conditions associated with the disease. In this study, distal symmetric polyneuropathy (DSPN) was identified as the most prevalent primary neurological disorder, followed by HIV-associated dementia (HAD) and acute inflammatory demyelinating polyneuropathy (AIDP), consistent with the findings of the NIMS study.(9) A total of five patients (5.49%) were diagnosed with a cerebrovascular accident (CVA). Among these, three patients exhibited an infarct in the basal ganglia, while the remaining two had an infarct in the cerebellum. The incidence of CVA in this study is in agreement with findings reported in other research.(16) DSPN can occur at any stage of HIV infection, although it is predominantly observed in individuals with CD4 counts below 200. Additionally, DSPN may result from the side effects associated with antiretroviral therapy (ART). In this study, ADC was identified in 6.59% of patients, diagnosed through the mini-mental state examination (MMSE). HIV infection typically results in a "subcortical" pattern of neurocognitive impairment, primarily affecting executive functions, information processing speed, attention and working memory, motor speed, the ability to learn new information, and the retrieval of that information. This condition is most frequently observed when the CD4 count falls below 100 cells/µL.(17) HIV/AIDS is well-recognized for its profound impact on the immune system, but its effects on the nervous system are equally significant. Neurological manifestations of HIV/AIDS can present in various forms, including cognitive impairment, motor dysfunction, and peripheral neuropathy, significantly affecting the quality of life for individuals living with the disease. Early treatment and prophylaxis of neurological problems in HIV patients are crucial to reducing the mortality rate.

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