

Neurological disorders in a consultant hospital in Northern Tanzania. A cohort study

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ABSTRACT

Objectives: To determine the sociodemographic characteristics, clinical findings and outcome by HIV status in a series of adult patients presenting with neurological disorders (NDs) and admitted to a consultant hospital in Northern Tanzania.

Methods: A cohort study took place over a 6-month period from Oct 2007 to March 2008 and included all adult patients with a neurological disorder admitted to the medical wards.

Results: A total of 1790 patients were admitted during this period, of whom 337 (18.8%) were diagnosed with a neurological disorder and formed the study group. Of these 337, 69 (20.5%) were HIV-positive. Among the 69 HIV positives, 25% were previously known to be HIV seropositive of whom 82% were on antiretroviral (ARV) medication. Seropositive patients were more likely than seronegative patients to be younger, better educated, have a business occupation, present clinically with confusion, headache and aphasia and have meningitis/CNS infection or a space occupying lesion. Seropositive patients were more likely to present with a Glasgow Coma Score (GCS) of 9–12/15 (33.3% v 17.2%). Seropositive patients had a median CD4 T-lymphocyte count of 47 cells/L and were more likely to be anaemic and have an elevated ESR. CT of the head was carried out on 132/337 (39%) patients. The overall findings were infarction 37%, hemorrhage 19%, tumors 15% and abscesses 9%. Brain abscess was more likely in seropositive patients and hemorrhage in seronegatives. The outcome at discharge for all patients was: death 27.6%, disability 54% and no disability 18.4% with death (39.1%) being more likely in seropositive patients. Patients presenting with coma (GCS < 9/15) were more likely to die whilst those with stroke, para/quadruplegia and space occupying lesions (SOLs) were more likely to be discharged with disability. Case fatality rate was highest for tetanus 71.4%, meningitis 57.1%, cerebral malaria 42.9% and CNS infections 37.1%. Seropositive patients presenting with meningitis and other CNS infections were more likely to die than seronegatives.

Conclusion: This study reports NDs occurring in one fifth of adult medical admissions with stroke and infections as the leading causes. The prevalence of HIV infection in NDs was 20%. The HIV positive cohort was characterized by advanced immunosuppression, CNS infections and high mortality.

1. Introduction

The overall burden of neurological disorders in hospitals in Africa is large. They account for up to 20% of medical admissions with infections, stroke, paraplegia and seizures as the leading causes [1–4].

Historically the main causes of CNS infections in Africa are acute bacterial meningitis, tetanus and malaria [5]. While these causes still remain, the overall pattern of CNS infections changed dramatically in Africa in the 1980s with the start of the HIV epidemic [6–8]. This change was mainly caused by opportunistic CNS infections occurring as

Abbreviations: ARV, antiretroviral; CNS, central nervous system; NDs, neurological disorders; KCMC, Kilimanjaro Christian Medical Centre; GCS, Glasgow coma score; HIV, Human Immunodeficiency Virus; SSA, sub-Saharan Africa; FBC, full blood count; ESR, erythrocyte sedimentation rate; CT, computerized tomography; OR, odds ratio; IQR, interquartile range; CFR, case fatality rate; WBC, white blood count; IRIS, immune reconstitution inflammatory syndrome; SOL, space occupying lesion

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a result of immunosuppression in HIV disease. The main causes are cryptococcus, toxoplasmosis, tuberculosis and acute bacterial infection [9]. Opportunistic infections became the most common cause of CNS infection in hospitalized adults and account for over 20% of all HIV related deaths in Africa [10,11]. The other leading causes of death in HIV infection in Africa are systemic tuberculosis, pneumonia and bacteraemia. Information on the role of HIV in the context of existing neurological disorders is limited in Africa, particularly in relation to their clinical features and outcome. In this paper we review a cohort of adult patients presenting with neurological disorders and admitted to a consultant hospital in Northern Tanzania and assess by HIV status their sociodemographic and clinical characteristics and outcome at discharge.

2. Patients and methods

This was a cohort study conducted in the medical department at Kilimanjaro Christian Medical Centre (KCMC), a consultant and teaching hospital located in Moshi town, Kilimanjaro region, Northern Tanzania. The study took place over a 6-month period from Oct 2007 to March 2008 and included all patients presenting with neurological complaints aged 13 years or above (this is the age cut off for admission to adult medical wards) who were admitted into the medical wards at KCMC. KCMC serves the Northern Zone involving six regions: Kilimanjaro, Tanga, Arusha, Manyara, Singida and Dodoma with a potential catchment population of over 16 million people. The hospital has an inpatient capacity of 500 beds out of which 87 are located in the medical department. Patients were seen and examined by SL and WH and in the majority of patients a distinct clinical neurological diagnosis was possible. Symptoms and signs were recorded for each patient. The following information was recorded for each patient: demographic data, symptoms, NDs, HIV status, CD4 count (if seropositive) and outcome. Outcome was defined as status on discharge and categorized as: death/disabled/not disabled. Disability was defined as 1) loss of function 2) requiring assistance with activities of daily living or mobility. We chose to use this simple definition of disability as this was not the main purpose of the study. A total of 337 eligible patients were identified and included in the study.

2.1. Laboratory investigations

Laboratory and imaging investigations were those carried out routinely at KCMC. These included haemoglobin, erythrocyte sedimentation rate (ESR) and CD4 counts. HIV test was done by two rapid HIV tests (Capillus/Bioline and Determine) and the results recorded for data analysis. Imaging investigations included Computerized Tomography (CT). A CT scan head scan was performed on patients suspected of having an abnormality but was limited in most cases to those patients who could afford to pay. The CT scans were interpreted and reported by an experienced radiologist.

2.2. Analysis

Statistical analyses were carried out using the software package SPSS version 12.0.1. (IBM Corp, Armonk, NY, USA). We analyzed patients separately by HIV status (HIV +/HIV-). When comparing mean age according to HIV status a Student's *t*-test was applied. For other variables, statistical significance was assessed using the chi-squared test or Fisher's exact test as appropriate. A *p*-value of < 0.05% was considered statistically significant. The odds ratios (ORs), with 95% confidence intervals (CIs), are also presented when comparing the prevalent proportions of the disorders between the two groups HIV +/HIV- and also the overall sociodemographic and clinical characteristics. However because the values for haemoglobin (Hb), and erythrocyte sedimentation rate (ESR) were not normally distributed, the Mann-Whitney *U* test was used to compare median values for HIV +/HIV-.

Table 1
Sociodemographic characteristics of patients with Neurological Disorders by HIV serostatus (*n* = 337).

Variable	Total	Serostatus		OR (95% CI)	p-value
		HIV-positive	HIV-negative		
		(Total = 69)	(Total = 268)		
		n %	n %		
Sex					
Male	176	34 (49.3)	142 (53.0)	1.0	
Female	161	35 (50.7)	126 (47.0)	0.9 (0.5–1.5)	0.682
Age group (years)					
13–24	36	3 (4.3)	33 (12.3)	1.0	
25–34	41	18 (26.1)	23 (8.6)	8.6 (2.3–32.6)	< 0.001
35–44	55	21 (30.4)	34 (12.7)	6.8 (1.8–25.0)	0.001
45–54	51	19 (27.5)	32 (11.9)	6.5 (1.8–24.2)	0.002
55–64	60	4 (5.8)	56 (20.9)	0.8 (0.2–3.7)	1.000
65–74	37	2 (2.9)	35 (13.1)	0.6 (0.1–4.0)	0.674
75 and above	57	2 (2.9)	55 (20.5)	0.4 (0.1–2.5)	0.372
Education level					
None	69	0 (0.0)	69 (25.7)	–	0.001
Primary	217	55 (79.7)	162 (60.4)	0.6 (0.1–2.4)	0.428
Secondary	43	11 (15.9)	32 (11.9)	0.6 (0.1–2.8)	0.668
Tertiary	8	3 (4.3)	5 (1.9)	1.0	
Region of residence					
Kilimanjaro	258	55 (79.7)	203 (75.7)	1.0	
Arusha	41	8 (11.6)	33 (12.3)	0.8 (0.4–2.0)	0.793
Tanga	16	3 (4.3)	13 (4.9)	0.8 (0.2–3.1)	1.000
Singida	9	2 (2.9)	7 (2.6)	1.0 (0.2–5.2)	1.000
Other	13	1 (1.4)	12 (4.5)	0.3 (0.0–2.4)	0.314
Occupation					
Subsistence farmer	156	12 (17.4)	144 (53.7)	1.0	
Employed	39	13 (18.8)	26 (9.7)	6.0 (2.5–14.6)	< 0.001
Business	66	29 (42.0)	37 (13.8)	9.4 (4.4–20.2)	< 0.001
Driver	6	4 (5.8)	2 (0.7)	24.0 (4.0–144.7)	< 0.001
Housewife	24	5 (7.2)	19 (7.1)	3.1 (1.0–9.9)	0.041
Student/pupil	18	1 (1.4)	17 (6.3)	0.7 (0.1–5.8)	1.000
Unemployed	10	2 (2.9)	8 (3.0)	3.0 (0.6–15.7)	0.201
Other	13	1 (1.4)	12 (4.5)	1.0 (0.1–8.3)	1.000

2.3. Ethical approval

Consent was sought from all participants or their close relatives after they had been informed of the purpose of the study. Participants completed Swahili or English versions of consent forms. Ethical clearance was obtained from the KCMC ethical committee. Confidentiality was adhered to when filling in data collection by using codes instead of names for identifying patients. For patients under 18 years of age, caretakers were asked to sign the consent forms on their behalf. Those who did not consent to participate in the study were given the same right for treatment as those who consented to be enrolled in the study.

3. Results

3.1. Sociodemographic

A total of 1790 patients were admitted into the medical wards between Oct 2007 and March 2008 of whom 337 (18.8%) presented with a neurological disorder and formed the study group. The main demographic characteristics are outlined in Table 1. There were 176 (52.2%)

Table 2
Main neurological symptoms by HIV serostatus ($n = 337$).

Presenting symptoms	Total	Serostatus		OR (95%CI)	p-value
		HIV-positive	HIV-negative		
		(Total = 69)	(Total = 268)		
		N (%)	N (%)		
Loss of consciousness	95	16 (23.2)	79 (29.5)	0.7 (0.37–1.39)	0.3
Hemiparesis	92	13 (18.8)	79 (29.5)	0.6 (0.27–1.12)	0.08
Confusion	70	26 (37.7)	44 (16.4)	3.1 (1.65–5.75)	< 0.001
Headache	55	22 (31.9)	33 (12.3)	3.3 (1.71–6.51)	< 0.001
Lower limb weakness +/- spasms	43	5 (7.2)	38 (14.2)	0.5 (0.16–1.32)	0.12
Seizures	41	7 (10.1)	34 (12.7)	0.8 (0.30–1.94)	0.565
Aphasia	37	12 (17.4)	25 (9.3)	2.1 (0.91–4.56)	0.056
Lower limb numbness	18	6 (8.7)	12 (4.5)	2.0 (0.65–6.12)	0.17

males and 161 (47.8%) females with a median age of 51 yrs., inter-quartile range (IQR) (36–67) years. A total of 69 (20.5%) were HIV-positive, of whom 17 (24.6%) were already known to be HIV seropositive whilst 52 (75.4%) were previously undiagnosed. Of the 17 patients with known HIV status 14 (82.4%) were on antiretroviral (ARV) medication. The mean age of HIV seropositive patients was 41.4 yrs. versus 54 yrs. for seronegatives ($p < .001$). Seropositive patients were also more likely to be better educated and have a business occupation.

3.2. Clinical features

The main presenting symptoms and neurological disorders and their relationship to serostatus are presented in [Tables 2 and 3](#). The Glasgow Coma Score (GCS) on admission was recorded for HIV positive versus HIV negative patients and results are as follows: < 9/15 (14.5 v 17.5%), 9–12/15 (33.3 v 17.2%), 13–14/15 (17.4 v 19.0%), 15/15 (34.8 v 46.3%). HIV-positive patients were significantly more likely to present with moderate coma; GCS 9–12/15 ($p \leq 0.004$), confusion, headache and aphasia and have the following neurological disorders: meningitis, CNS infections and space occupying lesions (SOL).

3.3. Laboratory and imaging features

The median CD4+ T-lymphocyte count in the 69 HIV seropositive patients was 47cells/L (IQR, 30–166), (78%: < 200 cells/L, 17%: 200–499 cells/L & 4%: > 500 cells/L). Patients who were HIV seropositive were more likely to be anaemic, median Hb 10.9 g% (IQR, 9.8–12.7, $n = 320$), and have an elevated ESR 65 mm/h. (IQR, 34–90, $n = 314$). A head CT was undertaken when indicated, and patients

could afford, and was carried out on 132/337 patients. Of these 50 (37%) had cerebral infarction, 25 (19%) hemorrhage, 20 (15%) tumors and 12 (9%) had abscesses. The relationship between HIV positivity and radiological diagnosis (brain CT scan) for abscess was significant (OR 22, (4.8–108.9, $p < 0.001$). Patients with hemorrhage were more likely to be HIV negative $p < 0.02$). Other diagnoses, 13(10%) included subdural hematoma, hydrocephalus, brain atrophy and calcifications. Normal CT scan findings were found in 17 (13%) patients.

3.4. Outcome

The overall case fatality rate (CFR) for patients with neurological disorders was 27.3% (93/337) as compared to 14.5% (259/1790) for all adult medical admissions as documented in the medical ward discharge registry during the same study period. The outcomes at discharge for HIV positive and negative patients are presented in [Fig. 1](#) and for individual NDs in [Table 4](#). Patients with infections, including tetanus, meningitis, cerebral malaria and other CNS infections were most likely to die. Patients with meningitis and other CNS infections who were seropositive were more likely to die than corresponding seronegatives. Patients with coma (GCS of < 9/15) were also more likely to die ($p < 0.001$). Patients with SOLs, stroke, and para/quadruplegia were more likely to be discharged with disability. Patients diagnosed to have associated medical disorders and epilepsy were least likely to be discharged with disability.

4. Discussion

Neurological disorders in this study accounted for about one fifth of all adult medical admissions similar to other published studies from

Table 3
Neurological disorder by HIV serostatus ($n = 337$).

Neurological disorders*	Total	Serostatus		OR (95%CI)	p-value
		HIV-positive ($n = 69$)	HIV-negative ($n = 268$)		
		N (%)	N (%)		
		N (%)	N (%)		
Meningitis	42	35 (50.7)	7 (2.6)	38.4 (14.8–103.5)	< 0.001
CNS infections	35	29 (42.0)	6 (2.2)	31.7 (11.6–91.3)	< 0.001
SOL	39	14 (20.3)	25 (9.3)	2.5 (1.1–5.4)	0.011
Stroke	129	5 (7.2)	124 (46.3)	0.1 (0.03–0.2)	< 0.001
Para/quadruplegia	37	4 (5.8)	33 (12.3)	0.4 (0.1–1.4)	0.126*
Seizures	19	0 (0.0)	19 (7.1)		0.017*
Cerebral malaria	14	1 (1.4)	13 (4.9)	0.3 (0.01–2.2)	0.32*
Tetanus	7	0 (0.0)	7 (2.6)		0.35*
Others	38	5(7.2)	33 (12.3)	1.8(0.7–4.8)	0.235
Associated medical disorders	21	1(4.8)	20 (7.5)	0.2(0.01–1.3)	0.09*

* Fisher's exact test.

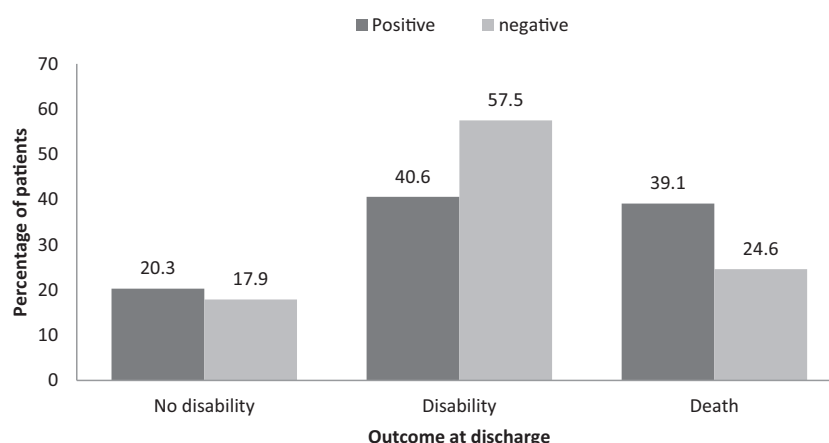


Fig. 1. Outcome by HIV status at discharge ($n = 337$).

Table 4

Neurological disorder by outcome at discharge ($n, 337$).

Neurological disorder	Total	Outcome			p-value
		Death	With disability	Without disability	
		No. (%)	No. (%)	No. (%)	
Meningitis	42	24 (57.1)	7 (16.7)	11 (26.2)	< 0.001
CNS infections	35	13 (37.1)	16 (45.7)	6 (17.1)	0.402
SOL	39	7 (17.9)	30 (76.9)	2 (5.1)	0.007
Stroke	129	32 (24.8)	87 (67.4)	10 (7.8)	< 0.001
Para/quadruplegia	37	7 (18.9)	30 (81.1)	0 (0.0)	0.001
Seizures	19	0 (0.0)	3 (15.8)	16 (84.2)	< 0.001
Cerebral malaria	14	6 (42.9)	3 (21.4)	5 (35.7)	0.039
Tetanus	7	5 (71.4)	0 (0.0)	2 (28.6)	0.01
Others	38	7 (18.4)	25 (65.8)	6 (15.8)	0.277
Associated medical disorders	21	8 (38.1)	2 (9.5)	11 (52.4)	< 0.001

Africa [1,4]. The frequency of HIV infection (20.5%) in NDs reported in this study is higher than the HIV seroprevalence reported among adult medical admissions (14%) to KCMC during the same time period and also reported in adults in the community (3.9%) in the local Kili-manjaro region. This confirms a strong association between NDs and HIV infection already noted in other studies in Africa [2]. The socio-demographic characteristics of HIV infection occurring more frequently in those in a younger age group, having a business occupation and better education are well known in Africa [8,9].

The overall clinical spectrum of NDs reported in this study is similar to that reported in the literature. It reflects the high burden of stroke, CNS infections and paraplegia as the most common NDs presenting to hospitals in Africa [1–7]. In a separate later study of causes of admission to KCMC for those aged 60 years and over, 24% had a stroke [12]. HIV positive patients in this study were significantly more likely to present clinically with altered GCS, confusion and headache and be diagnosed with meningitis and CNS infections. These results are similar to findings reported in South Africa [13]. In the present study there was a negative correlation of HIV infection with stroke. This may reflect the small number of HIV positive patients in the present study although this lack of association of HIV infection with stroke has previously been reported in South Africa [14,15]. However recent community-based studies from Africa, including one from Tanzania, suggest that HIV is a significant risk factor for stroke [16]. New onset seizures were present in 10% of HIV positive patients similar to findings from other studies [9,17].

The low median value of CD4 count of 47 cells/L, (78% < 200 cells/L) in HIV positive patients in this study indicates a cohort presenting

with an advanced level of immunosuppression. A similar pattern of low CD4 counts and advanced immunosuppression at clinical presentation is frequently reported in Africa and is considered to be the major risk factor for death in HIV [18,19]. Three quarters of the HIV positive patients in this study were previously undiagnosed demonstrating the high burden of unrecognized HIV disease in NDs in Africa.

The CT head findings in this study although restricted reflect the typical CNS disease pattern seen in NDs in a hospital setting in Africa with stroke, infections and space occupying lesions as the main causes. The association of HIV infection with brain abscess seen in this study is likely to be related to underlying cerebral toxoplasmosis or less frequently tuberculosis [13].

The overall in-hospital mortality rate in NDs in this study was 27.6% as compared to 14.5% reported in general medical inpatients admitted during the study period. A similar high mortality rate was reported by Winkler in Tanzania and by Bower in Ethiopia [3,4]. Mortality was highest in patients presenting with tetanus (71.4%), and meningitis (57.1%). A similar pattern of high mortality rates (> 50%) in tetanus and meningitis is reported from other studies in Africa [20–22]. The overall mortality in seropositive patients was 39.1%, being highest in infections: meningitis (54.3%) and CNS infections (37.9%) and SOL/abscess (21.4%). This agrees with other published studies from SSA showing high mortality rates varying from 50 to 60% in all cause meningitis to 20–30% in cerebral toxoplasmosis [18–22]. Advanced levels of immunosuppression with late clinical presentation, older age, high frequencies of immune reconstitution inflammatory syndrome (IRIS) and resource limited settings are the main risk factors for the high case fatality rate in HIV in SSA [18,19,23,24]. The higher than expected CFR (42.9%) versus an expected 10–15% in cerebral malaria may reflect inaccurate primary diagnosis in a resource limited setting or be a function of the small number of cases ($n = 6/14$) [25]. In this study > 50% of patients presenting with neurological disorders were disabled at discharge and this group included high proportions of stroke, space occupying lesions and para/quadruplegia. This underlines the significant role of NDs in contributing to the burden of long-term community-based disability.

5. Conclusion

This study describes the overall frequency, clinical characteristics and HIV prevalence (20%) in a cohort of adult patients presenting with NDs to a referral hospital in Northern Tanzania. Stroke, infections, SOL/abscess, paraplegia and seizures were the most common NDs. The prognosis was poor with 27% mortality and 54% morbidity at discharge. The HIV seropositive cohort was characterized by advanced immunosuppression, younger age group, CNS infection in particular meningitis and high mortality (39.1%).

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