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CENTRAL NERVOUS SYSTEM INFECTIONS IN THE RAINFOREST ZONE OF NIGERIA

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ABSTRACT

Objectives: **To ascertain incidence rates of central nervous system infections and provide information for health care planners.**
Design: **A two-stage screening through supervised case referrals and diagnostic evaluation at referral centre to establish a register of CNS infections.**
Setting: **A rural community in the rainforest zone of Nigeria with land area of 186500m^2, average daily temperature of 28°C, annual rainfall of 2080 mm, adult population of 109851 and served by 26 primary, three secondary and twelve comprehensive care facilities. More than two per cent of the populations live in waterlogged areas.**
Subjects: **Adults aged sixteen years and above, constituting incident cases of CNS infections.**
Main outcome measures: **Incident CNS infections per 100,000 populations averaged over a two year observational period.**
Results: **Incidence rates were 3.6, 4.1, 2.3, 09, 1.8, 0.9 for acute bacterial meningitis, aseptic meningitis, rabies encephalitis, non-rabies encephalitis, tuberculous meningitis and chronic non-tuberculous meningoencephalitis, respectively. Syphilitic neuroarthropathy had 0.46.**
Conclusions: **Mortality from acute pyogenic meningitis and tuberculous meningitis remained distressingly high. Aseptic meningitis had the highest incidence rate, yet remained inadequately emphasised. Rabies encephalitis was the third commonest cause of CNS infection in the area.**

INTRODUCTION

Infections of the central nervous system (CNS) contribute significantly to the morbidity and mortality of central nervous system diseases in tropical and sub-tropical world. Studies from major centres in Africa showed a hospital incidence of 19-46% of all neurological problems(1-3). The causative agents of these infections reach human population by passing through diverse environmental factors. In Nigeria, amoebic encephalitis and epidemic meningitis occur in the northern Savannah within the meningitis belt of sub-Saharan Africa(4,5). In the southern tropical rainforest zone, meningitis occurs largely as sporadic cases(6,7).

Population-based studies of CNS infections in developing countries are few. Most hospital-based data concern largely urban and sub-urban population(5,8,9). Available information from population studies suggested frequencies of 3, 4, 2, 0, 8, 1 -per 100,000 for septic, aseptic, tuberculous meningitis and encephalitis respectively(10).

Ihiala local government area (LGA) of Anambra State Nigeria has operated and expanded its primary health care system based on the policy guidelines of the federal ministry of health. An efficient communication network organised by the missionary workers (Congregation of the Immaculate heart Sisters and the Catholic Mission), local government health visitors and community health officers ensure dissemination of health information to village dwellers. This largely rural population was enumerated in the most recent national population census and has a figure of 109851 for its adult population (1991 census) 16 years and above. The present report is a descriptive epidemiology of CNS infection in Ihiala LGA a rural population in the rainforest zone of the south-eastern part of Nigeria. The study spanned through a 24-month period ending 30th October 1993.

MATERIALS AND METHODS

Ihiala LGA is situated about 64 kilometers south of Onitsha (itself on the eastern Niger basin some 198 km south of the confluence of the rivers Niger and Benue), and has a land area of about 186500m^2, with about 2.5% of its population living around small tributaries of the river Niger in water logged areas throughout the rains. The average daily temperature is about 28°C and the annual rainfall of the local government area is about 2080 mm.

The medical facilities in the LGA consisted of: governmental facilities including: twenty primary health care centres (PHC) and manned by health officers and community midwives; one comprehensive health centre (CHC) manned by a general medical practitioner; two general hospital (GH) and manned by general

medical practitioners) and non governmental facilities (including: six maternity centres (M.C.) manned by state registered post basic nursing midwives; privately owned hospitals and clinics eleven manned by qualified medical doctors; one voluntary agency mission hospital - the Our Lady of Lourdes Hospital (OLLH).

The OLLH is a 250 bed catholic mission hospital (with capacity for expansion) offering: specialist consultant services in internal medicine, surgery and obstetrics; intensive care unit services and training schools for nurses, midwives, laboratory assistants and pre-registration medical officers. It is a major referral centre for the other health institutions in the LGA and beyond. Its central location offered additional communication advantages.

Effective communication and information dissemination about the study was achieved by the existing network, (mentioned earlier), largely through group contacts. Community health officers and community midwives at the PHC, CHC and MC were recruited at the outset and trained on recognition, (of febrile illnesses and disorders associated with impaired consciousness) documentation, and subsequent direct referral of cases to the OLLH. Similarly, before the study took off, personal visits were paid to the general practice clinics and the general hospitals to discuss case recognition and direct referrals with the doctors in charge of the clinics and hospitals. Continuity was ensured by regular visits to these centers, the personnel on ground were guided on recognition and documentation of cases. Five centres were visited each week. The CHC and the general hospitals were visited weekly to enable the researchers join these centres in their scheduled weekly clinical activities review. Centres that were in close neighbourhood were visited the same day. On the average each centre was visited at least once in five weeks.

The primary patients' data which were entered into a proforma, together with the patient were transferred to the OLLH accompanied by personnel from these peripheral centres. The patients were seen by the attending emergency room doctor and subsequently by a member of the study team (CM), and were thereafter admitted. A clear history of an illness characterised by fever, and/or headache with meningeal signs with or without progressively impaired consciousness, of acute, sub-acute or insidious onset were sought for. A detailed physical examination including neurological examination was performed by one of the investigators (CM). A lumbar puncture was performed in all cases except when a brain abscess was being considered and fundoscopy showed evidence of papilloedema. The cerebrospinal fluid (CSF) obtained were analysed for protein, glucose, cellular content, and cultures for bacterial isolation. Ziehl-Nielsen stains for acid-fast bacilli, Gram and Indian ink stains of spun CSF samples were also done. Blood cultures were done in all cases. Blood and CSF serological examinations, venereal diseases research laboratory (VDRL), *Treponema pallidum* haemaglutinaton test (TPHA), HIV-1 and 2 immunocomb bispot tests)-were also done (NAUTH Haematology Immunology laboratory). Other viral studies and isolations were not carried out. Routine laboratory studies on admission included complete blood count, random blood sugar, serum urea, creatinine and electrolytes, erythrocyte sedimentation rate, liver function tests, urinalysis and cultures of catheter specimens of urine. All patients had a chest radiograph done at OLLH. Computer tomographic studies were done in two cases in a tertiary referral centre.

The EEG examinations were done in selected cases before discharge of the patients. The following diagnostic criteria were used for the various categories: (i) acute pyoyenic meningitis was diagnosed according to the criteria set out by Dada and Jaiyeola(6) - (namely, any three of the following: purulent CSF; large numbers of polymorphonuclear leucocytes in CSF; protein content of not less than 60mg/dl of CSF; CSF sugar of less than 40mg/dl; Isolation of causative bacteria - are diagnostic); (ii) aseptic meningitis (ASM), and encephalitis were diagnosed using the criteria set by Adams and Victor(11); (iii) brain abscess was diagnosed when in addition to the systemic inflammatory response; - there was clinical evidence of space occupying lesion in the brain; focus for purulent metastatic spread (blood, heart, lungs) elsewhere; and clinical evidence of lateralising neurological signs; (iv) tuberculous meningitis was diagnosed when the disorder showed a chronic course, the CSF examination showed predominantly lymphocyte pleocytosis, elevated protein with low sugar content, a positive Mantoux test was obtained with or without recovery of tubercle bacilli in the CSF, and progressive recovery with antituberculous treatment; (v) central nervous system syphilis was considered when both blood and CSF showed positive results with both VDRL and TPHA and; (vi) permission for post mortem were denied mostly on cultural grounds, except in one case in which a limited necropsy (post mortem LP) was granted.

Information provided by the primary data forms was doubly checked by the investigators and along with findings on physical examination and diagnostic procedures were entered into a register of infections and diseases causing impaired consciousness. Incidence rates were expressed per 100,000 adult populations per year.

RESULTS

Eight cases of acute pyogenic meningitis were encountered during the two year period. *Diplococcus pneumonia* was isolated from the CSF in five of them, while *Neisseria meningitides, E. coli* and *S. typhi* were isolated from the CSF each in one patient only. Two patients with pneumococcal meningitis, and two others with meningococcal and *E. coli* meningitis died. One patient with pneumococcal meningitis recovered with deafness while the other three recovered without any residual neurological deficit. Two of them had normal brain scans at subsequent follow up (Table 1).

The CSF showed lymphocyte pleocytosis, elevated protein (with clot webs in two patients) and low glucose in all four patients with tuberculous meningitis. Acid-fast bacilli was identified in the CSF smear in one of them. There were no facilities for culture of the CSF for tubercle bacilli. Two of the patients who had papilloedema on admission also had abducens nerve palsy. One of the latter group (a male) and another (a female) with multiple cranial nerve (iii, iv, vi, xii) involvement developed focal seizures involving their left upper extremity during the course of admission. The females asphyxiated and died suddenly five weeks after admission following aspiration of gastric contents during an episode of Jacksonian march and the subsequent generalised convulsion. One of the male patients developed adult respiratory distress syndrome and died six days after admission. Another male patient

Table 1

Distribution of patient with CNS infections according to age and diagnosis

Diagnostic category	Age range (yrs)	Sex frequency M	F	% of total	Incidence rate per 100,000 adult population	Outcome D	S
Acute bacterial meningitis	18 - 85	3	5	24.2	3.6	4	–
Aseptic meningitis	17 - 43	3	6	27.3	4.1	1	8
Encephalitis (rabies)	16 - 56	2	3	15.1	2.3	5	–
Encephalitis (non-rabies)	17 - 42	0	2	6.1	0.9	1	1
Tuberculous meningitis	16 - 65	3	1	12.1	1.8	3	1
Chronic meningitis (non tuberculous	50 - 53	1	1	6.1	0.9	2	–
Neuroarthropathy	63	1	0	3.0	0.46	–	1
Brain abscess (non-trauma related)	17 - 19	2	0	6.1	0.9	1	1
Total		15	18	100		17	16

Incidence rates are 100,000 populations per year aged 16 years and above
M = male: F = female; D = died; S = survived

developed the syndrome of inappropriate anti-diuretic hormone secretion after initial improvement with treatment. He had progressive confusion and hyponatraemia without oedema and hypertension, and died from cardiopulmonary arrest following an episode of generalised convulsion. The only surviving patient in this category was discharged to follow up with spastic paraparaesis after six months of admission. None of these patients had co-existing HIV infection.

The unavailability of viral cultures made it difficult to prove viral aetiology in the patients with aseptic meningitis. However one of the patients showed positive results with immunocomb HIV-bispot screening. This was confirmed by the Western blot test. He died in the course of the admission.

The CSF of the nine patients with aseptic meningitis contained between 40-960 leucocytes per mm^3. In all but one of them the CSF protein was elevated. The eight other patients with aseptic meningitis recovered uneventfully. In the two patients with probable viral encephalitis (non rabies) one had 32 and the other had 98 leucocytes per mm^3 in their CSF. The former developed haemorrhagic features and was thought to have viral haemorrhagic fever. She died six days after admission. The other recovered uneventfully. Five patients had rabies encephalitis of the furious type. Two of them who were sibs were bitten by the same dog. The others also had dog bites. All the five patients died.

Two patients had predominantly lymphocyte (350 and 20/mm^3) pleocytosis in the CSF. Their CSF proteins content were 60 and 96mg per dl with normal levels of glucose. Both showed fluctuating physical signs with waxing and waning of levels of consciousness, all through admission. Both CSF specimens grew no bacteria. Both patients had taken medications for between seven and 12 days at home before presentation, but the identities of these medications were unknown. Repeated lumbar CSF examination suggested pneumococal meningitis (by latex agglutination) in one but not in the other. Both patients died (despite antimicrobial therapy with ceftriaxone, chloramphenicol and gentamicin) in their 4th and 5th admission weeks. The causes of their chronic meningitis remained undetermined.

One patient with CNS syphilis had spinal neuroarthropathy. Both the VDRL and the TPHA tests were positive in the blood and CSF. Two young adult male patients developed brain abscesses. One of them was following chronic suppurative otitis media (CSOM), the other as a complication of infective endocarditis. Blood cultures were negative in the patient with CSOM while in the patient with infective endocarditis *Staphylococcus aureus* was isolated from the blood. Both patients were referred to a neurosurgical unit. The EEG examination in the patients with CSOM showed right temporal delta and sub delta paroxysms. He had a right carotid angiogram (which showed a right temporal mass lesion) and eventual surgical evacuation. The second patient died during transit to the surgical unit.

DISCUSSION

The real incidence of acute bacterial meningitis in developing countries continues to present challenging problems. Elsewhere the commonly quoted incidence rate is four to five per 100,000 populations(12). In the present study, we found an incidence rate of 3.6 per 100,000 populations. Radkrishnan found a lower incidence rate of two per 100,000 in Benghazi Lybia(10). Several epidemiological studies involving all age groups showed a preponderance of pyogenic meningitis in childhood(5,13-15).

The pneumococcus was the commonest organism causing bacterial meningitis in the present study. This finding agrees with that of Radkrishnan(10) and that of other epidemiological studies(6,15), The overall attack

rate of pneumococcal meningitis worldwide is 1-2 per 100,000, with the rate increasing among elderly patients(16). The age range of the patients encountered in our study (18-85 years) may be partly responsible for the higher rates observed.

The clinical syndrome of viral (aseptic) meningitis is poorly emphasised in many developing countries. This probably is attributable to inadequate facilities for viral studies and tendency to spontaneous recovery in many patients with mild illnesses. In the present study we found a yearly incidence rate of 4.1 and 0.9 per 100,000 persons, for aseptic meningitis and non-rabies encephalitis respectively. Studies from Helsinki showed incidence rates of 2-4 per 100,000 for viral encephalitis while aseptic meningitis occurred 10 times more frequent(17). In the Libyans study, rates of 1 and 3.4 per 100,000 persons for encephalitis and ASM respectively were found(10). Rabies encephalitis presented a unique problem in our study. The endemicity of rabies remains to be determined in the study location. Sporadic and near epidemic outbreaks do occur in the area, frequently in the dry seasons. The reasons for this tendency remain unclear but may not be unrelated to the increased exposure of hunting dogs to wild rabies virus, during hunting expeditions - a seasonal occupation that is common among young and older adults in the location. The incidence of rabies encephalitis in our study doubled that of non-rabies encephalitis (ratio of 2.5:1).

Tuberculous meningitis has continued to be an important cause of morbidity and mortality in developing countries where poverty and sub-standard sanitary conditions prevail. Although none of the patients in the present study had co-existing HIV infection, the rising incidence of CNS tuberculosis in the era of HIV pandemic are indications that tuberculous meningitis may become increasingly important incident in CNS infections worldwide.

Meningovascular syphilis has been said to be commoner in Africa when compared to spinal cord involvement(18). In the present study we found only one case of neuroarthropathy. The insufficient number of patients with proven syphilis does not permit further comparison of the incidences of its various forms of CNS involvement. Partially treated pyogenic meningitis may present sub-acutely with evidence of ventriculitis, communicating or non-communicating hydrocephalus and multiple cranial nerve palsies(19). Two of the patients encountered in the present study showed waxing and waning of symptoms. Although latex agglutination of CSF sample suggested a pneumococcal origin, repeated CSF cultures were negative. Bacterial origin of CNS infection in these two patients was inconclusive. Fungal studies were not done, as these tests were unavailable. Thus the aetiology of the CNS infection in these cases remained undetermined.

Two cases of non-trauma related brain abscesses were seen in the present study. Abscesses in the brain are most commonly secondary to suppuration elsewhere in the body(19). The aetiologic agents were found in the majority of the cases; in others the agents elude identification. *S. aureus* was isolated from the blood culture in one of the patients in this study. An incidence rate of 0.9 per 100,000 may be underestimation of the actual rates as most of the patients may present to other centres with the primary suppurative lesions. Nevertheless its presence in the locality calls for a high index of suspicion among patients with predisposing suppurative lesions, thus avoiding the bleak outcome of undiagnosed brain abscess.

The mortality rate in the present study of 51.5% remains distressingly high and probably reflects inadequate prompt interventional measures and delays before presentation.

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