Profile of Tuberculous Meningitis with or without HIV Infection and the Predictors of Adverse Outcome
SK Bandyopadhyay1, R Bandyopadhyay2, A Dutta3

ABSTRACT

Objectives: To compare the clinical, radiological and cerebrospinal fluid (CSF) findings, at hospital admission, among adult patients with tuberculous meningitis (TBM) with or without HIV infection and to identify the factors that predict adverse outcome at six months.

Methods: A total of 82 adult patients with TBM were included (40 HIV-positive and 42 HIV-negative). Several clinical (duration of illness, Glasgow Coma Scale score, presence of high temperature, headache, cranial nerve or sphincter abnormality, seizures and endocrine dysfunction), radiological (presence of hydrocephalus, cerebral infarction and oedema, meningeal enhancement, granuloma) and cerebrospinal fluid parameters (glucose, protein, lactate, lymphocytes, neutrophils and adenosine deaminase values) were recorded along with CD4 count in the peripheral blood. Statistical analysis was performed using the chi-square test. Individual variables were evaluated as prognostic factors for adverse outcome in both groups by calculating the relative risk of association for each.

Results: Temperature more than 38.33°C was more common in the HIV-negative group while seizures, hydrocephalus, cerebral infarction and low CD4 count occurred significantly more commonly in the HIV-positive group. Hydrocephalus had strong association with severe neurological deficit and seizure with death in both the groups.

Conclusion: Several clinical and laboratory features of TBM in patients who are HIV-positive are distinctly different from those without HIV infection; some of these have an association with the probability of adverse outcome.

Perfil de la Meningitis Tuberculosa con o sin Infección por VIH y Predictores de la Evolución Clínica Adversa
SK Bandyopadhyay1, R Bandyopadhyay2, A Dutta3

RESUMEN

Objetivos: Comparar los hallazgos clínicos, radiológicos y del líquido cefalorraquídeo (LCR) entre pacientes adultos con meningitis tuberculosa (MTB) con o sin infección de VIH en su ingreso al hospital, e identificar los factores que predicen la evolución clínica adversa en seis meses.

Métodos: Un total de 82 pacientes adultos con MTB fueron incluidos (40 VIH positivos y 42 VIH negativos). Se registraron varios parámetros: clínicos (duración de la enfermedad, puntuación de la Escala de Coma de Glasgow, presencia de alta temperatura, dolor de cabeza, anormalidad del esfínter o nervio craneal, o anormalidad del esfínter, convulsiones y disfunción endocrina); radiológicos (la presencia de hidrocefalia, infarto cerebral, edema, realce meningo, granuloma); y del líquido (glucosa, proteína, lactato, linfocitos, neutrófilos, y valores de adenosina deaminasa), junto con un conteo de CD4 en la sangre periférica. Se realizó un análisis estadístico usando la prueba de chi-cuadrado. La variable individual se evaluó como factor pronóstico de la evolución clínica en ambos, calculando el riesgo relativo de asociación para cada uno.
INTRODUCTION
Tuberculosis remains an endemic disease in developing countries. Diagnosing tuberculous meningitis (TBM) when the patient first presents is still fraught with difficulties and patients are often treated empirically on clinical suspicion before proof of tuberculosis is obtained. The incidence of severe cases, which include miliary tuberculosis, tuberculous meningitis and extrapulmonary tuberculosis are high among HIV-associated tuberculosis cases (1). Conversely, the association of tuberculosis with HIV is a poor prognostic factor in HIV infection (1). As the acquired Immune Deficiency Syndrome (AIDS) epidemic is expanding at an alarming rate, the combination of HIV and tuberculosis may be devastating (1).

AIM
The aim of the study is to compare the clinical, radiological and cerebrospinal fluid (CSF) findings of adult patients with TBM who were HIV-positive with those who were HIV-negative. An attempt was also made to identify the predictors of adverse outcome (death or severe neurologic deficit) at six months in these two groups of patients.

SUBJECTS AND METHODS
Over a period of three years (from January 2004 to December 2006), all the patients with proven or clinically probable TBM who were admitted in the Indoor Wards of our hospital were recruited into the study. A total of 82 patients were included of which 40 were HIV-positive. When either CSF cultures for tuberculosis or polymerase chain reaction (PCR) for tuberculosis were positive or Ziehl-Neelsen (Z-N) staining showed acid fast bacilli (AFB), the case was classified as definite TB meningitis. All other patients who had tuberculosis at another site with characteristic clinical and CSF findings, or known previous tuberculosis who improved on antituberculous treatment coupled with characteristic clinical and CSF findings were classified as highly probable TBM.

The patients were evaluated clinically and chest X-rays (CXR), contrast-enhanced computed tomography (CECT) scan of the brain, CSF profiles, HIV serology and routine blood tests were done at the time of hospital admission. The HIV status was determined by enzyme linked immuno-sorbent assay (ELISA) and confirmed by Western blotting where possible.

RESULTS
Comparison of clinical, biochemical and radiological parameters are shown in Table 1. Mean age of the patients was 32.8 years in patients who were HIV-positive and 36.1 years in those HIV-negative. Average duration of illness and mean GCS score was also comparable between the groups. Amongst the clinical symptoms, a temperature reaching > 38.33°C at admission was more common in patients who were HIV-negative and the occurrence of seizures was more common in HIV-seropositive individuals while the incidence of cranial nerve abnormality, sphincter abnormality, and

Resultados: Una temperatura de más de 38.33°C fue más común en el grupo VIH negativo, mientras que convulsiones, hidrocefalia, infarto cerebral, y bajo conteo de CD4 ocurrieron significativamente más normalmente en el grupo VIH positivo. La hidrocefalia estuvo fuertemente asociada con un déficit neurológico severo y la convulsión con la muerte en ambos grupos.

Conclusión: Varias características clínicas y de laboratorio del MTB en pacientes que son VIH positivos, difieren claramente de aquellos con infección por VIH. Algunas de estas características se hallan asociadas con la probabilidad de una evolución clínica adversa.

endocrine dysfunction were not significantly different between the groups. On CECT of brain, hydrocephalus and cerebral infarction were more commonly associated with HIV infection. However, meningeal enhancement, granuloma and cerebral oedema were equally prevalent in both groups. Neither of the CSF criteria evaluated showed any significant difference between the two groups. In patients who were HIV-positive, the mean CD4 count was 184/µm³ (with 60% having a value of < 200/µm³) compared to 558/µm³ in patients without HIV infection (p < 0.01).

On independent risk factor analysis in patients with HIV infection, a GCS score of less than 9/15, occurrence of seizures and a CD4 count of less than 200/µm³ were strongly associated with mortality while the presence of hydrocephalus and cerebral infarction in CECT and cranial nerve involvement on clinical examination were associated with SND (Table 2). In individuals who were HIV negative, the relative risk of death was more in those with seizures and CSF glucose less than 30 mg/dL. Presence of hydrocephalus on cranial CT showed a strong association with SND in this group (Table 2). However most patients with (70%) or without (~90%) TBM did not present with seizure. Only three patients had seizure with temperature > 38.33°C in the HIV-seropositive group; their mean CD4 count was 213/µm³.

### DISCUSSION

In this study, the aim was to analyse clinical, radiological and CSF findings in TBM cases to evaluate whether HIV infection significantly influences the characteristic findings. The results showed that most of the patients who were HIV-positive were in the AIDS portion of the HIV spectrum (CD4 count < 200/µm³). They failed to mount a significant rise in temperature owing to underlying immunosuppression and had seizures more commonly due to the presence of a gamut of subclinical CNS diseases (opportunistic infections as well as noninfectious causes). Also hydrocephalus and cerebral infarction were more common in them. Co-existing HIV encephalopathy, opportunistic infections and extensive vasculopathy probably contributed to such radiological findings. Notwithstanding previous reports (2), HIV infection in the patients did not significantly altered the presenting CSF findings.

Berenguer et al reported that infection with HIV does not appear to change the clinical manifestations or the outcome of TBM (3). Similar results were found by Bossi et al (4). In a study from South Africa, clinical and CSF findings were similar in HIV-infected and uninfected TBM patients but ventricular dilatation and infarcts were more frequent in patients who were HIV-positive and GCS was a better indicator of prognosis than CD4 count (5). Similar to our observations, one group from India found that many of the clinical, radiological and pathological features of TBM in patients who were HIV-positive was distinctly different from those without HIV infection (6).

The presence of hydrocephalus is an established risk factor for poor outcome in TBM patients while a low GCS score is a predictor of 6-month outcome in HIV-infected patients (2, 7). In addition, disease severity at admission,
presence of focal weakness, prolonged somatosensory evoked potential and absence of corticosteroid use had been shown to be associated with death or poor prognosis in various analyses (7, 8).

REFERENCES