

Original Research Article

Pattern of HIV infected meningitis patient investigated in a tertiary care institute of eastern India

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ABSTRACT

Background: This study was started in the aim of determining the pattern of meningitis and their clinico-laboratorial presentation among HIV infected patients.

Methods: This secondary data based cross-sectional study was conducted on 2010 in a tertiary care institute of eastern India among HIV infected meningitis patients. From June 2009 to May 2010, 92 patients were included in our study. Bed head tickets, laboratory reports and registers were used for data collection. Chi square test was applied for the test of significance.

Results: 70.7% cryptococcal and 29.3% tubercular meningitis cases were found. Mean CD4 cell count, CSF protein, CSF glucose, WBC cell count of TB and cryptococcal meningitis patients were 143 cells/cumm, 546.1 mg/dl, 26.8 mg/dl, 550 cells/ cumm and 175 cells/ cumm, 189.1 mg/dl, 30.1 mg/dl, 36 cells/ cumm respectively. 29.2% patients of Cryptococcal meningitis were presented with mental change, confusion or psychological disorders, but these symptoms were not observed among TB meningitis patients.

Conclusions: This study provided a baseline data about epidemiology and clino-laboratorial features of HIV meningitis patients of eastern India and will help for further investigation in this field.

Keywords: HIV, CD4 count, Cryptococcal meningitis, TB meningitis

INTRODUCTION

In 21st century Human Immune deficiency virus (HIV) infection is the deadly pandemic disease for the world. According to UNAIDS 2016 report, there were 36.7 million people living with HIV in the world.¹ Non curable outcome and fatal manifestations of the disease make it deadly. HIV patients are susceptible to many opportunistic diseases due to its immunosuppressive nature. Meningitis is one of them and fatal and deadly also in respect to disease outcome.^{2,3} Most of the cases of meningitis among HIV infected patients are the result of opportunistic infection instead of HIV virus itself. Different forms of meningitis are associated with HIV

infection. Cryptococcal and tubercular meningitis are common etiological variant in HIV-endemic areas.^{2,4,5} Evidence revealed that cryptococcal meningitis is the most common fungal meningitis as well as common opportunistic infection of meninges in patients living with HIV.^{3,6-9} TB meningitis was described as second most common cause of meningitis among HIV-infected individuals, with 67% case fatality rate.^{5,10,11}

Currently in Eastern India zone, data regarding the prevalence of specific microbiological agent in CSF (Cerebro spinal fluid) and clinical presentation of meningitis among HIV patients are not well documented yet. To find out the way of prevention, it is necessary to

understand the HIV-meningitis case presentations in depth respect to this geographical context.

In this background the present study was conducted to determine the pattern of meningitis and their clinico-laboratorial presentation among HIV infected patients in the aim of exploring the baseline data regarding HIV-meningitis for the betterment of patient's care.

METHODS

This secondary data based cross-sectional study was conducted on 2010 in the department of Microbiology, Calcutta School of Tropical Medicine, West Bengal, India. It is a renowned tertiary care institute of India with historical values. It is situated in the same premises of Calcutta Medical College, Kolkata, which is Asia's 1st Medical College of modern science. All the HIV diagnosed patients who were suffering from Meningitis and admitted to this Hospital were considered as our study population. From June 2009 to May 2010 all hospital admitted HIV meningitis patients were included in our study. Patients who had incomplete information regarding the study were excluded from the study. Patients were excluded mainly due to dying before performing CSF examination or having contraindication to lumbar puncture, contaminated or inadequate CSF sample and inadequate patient's information about clinical conditions. Ultimately 92 patients were included in our study and 5 were excluded for different reasons. HIV meningitis patients were identified and confirmed by reviewing of bed head tickets where clinician's diagnoses were written clearly. Socio-demographic and clinical data of the admitted patients were obtained from bed head tickets. Their CSF study reports were tracked and collected from the registers of the Microbiology department. CSF reports which were positive for Cryptococcus were examined thoroughly including antigenic titer in Mycology division under the Microbiology department.

CSF sample: CSF was collected aseptically by lumbar puncture and physical study done.

Sample processing: CSF was then centrifuged at 2000 rpm for 10 minutes.

Diagnostic methods for cryptococcal meningitis

Direct examination: One part of pellet was stained by India ink and then directly examined under microscope.

Culture: Another part of the pellet was cultured on Sabouraud dextrose agar media (SDA) and then incubated at 37⁰ C for 5-8 days. Another culture medium i.e. Niger seed agar was also used which showed brown coloured colonies after incubation at 22-25⁰ C for 3-5 days.

Identification: Biochemical test like production of urease was performed for the detection and identification of *Cryptococcus neoformans*.

Diagnostic methods for Tubercular meningitis

Smear prepared from the centrifuged deposit was stained by modified Ziehl-Neelsen method: Acid fast bacilli (AFB) was present.

Culture: Centrifuged deposit was then inoculated in Lowenstein-Jensen (LJ) media and incubated at 37⁰C for 6-8 weeks. Colonies formed on LJ media are identified using standard protocol for identification.

Cell count: One part of unspun CSF was used for cell count and cell type.

Ethical permission was obtained from Institutional review board.

Data were entered in Microsoft Excel worksheet (Microsoft, Redwoods, WA, USA) and were analyzed using IBM SPSS software, version 19.0 (Statistical Package for the Social Sciences Inc, Chicago, IL, USA) and Microsoft Excel.

Chi square test were applied for the test of significance in accordance to applicability. Pearson's Correlation test was used to observe the association between two quantitative variables. P value <0.05 was considered for statistical significance.

RESULTS

Among 92 HIV meningitis patients 70.7% were suffering from cryptococcal meningitis and rest were suffering from tubercular meningitis. Only this two variant of meningitis were found among admitted patients (Table 1).

Table 1: Distribution of HIV meningitis patients according to type of meningitis (n=92).

Type of meningitis	Number (%)
Cryptococcal meningitis	65 (70.7)
TB meningitis	27 (29.3)
Total	92 (100)

Among the young adult (18-40 years) HIV patient cryptococcal meningitis cases (81.7%) were found significantly more than tubercular meningitis cases (48.1%). Maximum tubercular meningitis patients (51.9%) were observed in middle adulthood age (41-60 years). Proportion of female patients was found significantly more among cryptococcal meningitis patients (38.5%) compare to tubercular meningitis cases (14.8%).

Mean CD4 cell count of TB and cryptococcal meningitis patients were 143 cells/cumm and 175 cells/cumm respectively. HIV patients who had CD4 count ≤ 50 /cumm chances of tubercular meningitis significantly increased than cryptococcal meningitis. This is shown by significant Chi square test.

CSF study of the HIV meningitis patients revealed that most of the cryptococcal meningitis patients (56.9%) had CSF protein up to 100 mg/dl and all tubercular meningitis patients had CSF protein above 100 mg/dl. This finding is statistically significant also. Mean value of CSF protein of TB and cryptococcal meningitis patients were

examined 546.1 mg/dl and 189.1 mg/dl respectively. Proportion of meningitis patient, who had CSF glucose level up to 45 mg/dl, was found significantly more among tubercular variant (92.6%) compare to cryptococcal variant (72.3%). Mean value of CSF glucose of TB and cryptococcal meningitis patients were observed 26.8 mg/dl and 30.1 mg/dl respectively. In most of the cases of TB meningitis (92.6%) had CSF cell count more than 5 cells/cumm and significantly higher compare to cryptococcal meningitis (64.6%). In CSF study we found 550 cells and 36 cells per cumm CSF in average among TB and cryptococcal meningitis patients respectively (Table 2).

Table 2: Distribution of HIV meningitis patients according to socio-clinical factors and laboratorial parameters of CSF (n=92).

Variables	Subvariable	TB meningitis (%)	Cryptococcal meningitis (%)	Total (%)	Test of significance
Age (in years)	18-30	4 (14.8)	4 (6.2)	8 (8.7)	Chi square test $\chi^2=18.006$, df=3, p=0.000*
	31-40	9 (33.3)	49 (75.5)	58 (63)	
	41-50	11 (40.8)	12 (18.5)	23 (25)	
	50-60	3 (11.1)	0 (0)	3 (3.3)	
Gender	Male	23 (85.2)	40 (61.5)	63 (68.5)	Chi square test $\chi^2=4.942$, df=1, p=0.026*
	Female	4 (14.8)	25 (38.5)	29 (31.5)	
CD4 count	≤ 50 /cumm	8 (29.6)	3 (4.6)	11 (12)	Chi square test $\chi^2=13.989$, df=3, p=0.003*
	51-100/cumm	7 (26)	32 (49.2)	39 (42.4)	
	101-500 /cumm	9 (33.3)	27 (41.6)	36 (39.1)	
	>500 /cumm	3 (11.1)	3 (4.6)	6 (6.5)	
CSF protein	Up to 100 mg/dl	0 (0)	37 (56.9)	37 (40.2)	Chi square test $\chi^2=31.554$, df=2, p=0.000*
	101-500 mg/dl	16 (59.3)	24 (36.9)	40 (43.5)	
	>500 mg/dl	11 (40.7)	4 (6.2)	15 (16.3)	
CSF glucose	Upto 45 mg/dl	25 (92.6)	47 (72.3)	72 (78.3)	Chi square test $\chi^2=4.614$, df=1, p=0.032*
	46-80 mg/dl	2 (7.4)	18 (27.7)	20 (21.7)	
CSF cell count	0-5/ cumm	2 (7.4)	23 (35.4)	25 (27.2)	Chi square test $\chi^2=7.545$, df=1, p=0.006*
	>5 / cumm	25 (92.6)	42 (64.6)	67 (72.8)	

All above findings were found statistically significant in Chi square test. Phi and Cramer's V tests showed moderate level of strength of association in above tests.

Bivariate Pearson's correlation test showed that cryptococcal antigen titre value had no statistical significant relationship with the patient's CD4 count.

In case of both type of meningitis headache and fever were most common presenting symptoms. Among cryptococcal meningitis patients 29.2% were presented with mental change, confusion or psychological disorders, but TB meningitis patients had no similar type of symptoms. Neck stiffness was observed mostly among cryptococcal meningitis cases (40%) and very few among TB meningitis (3.7%) (Table 3).

Table 3: Distribution of HIV meningitis patients according to their presenting symptoms (n=92).**

Symptoms	TB meningitis (%) (n=27)	Cryptococcal meningitis (%) (n=65)
Headache	27 (100)	65 (100)
Fever	22 (81.5)	65 (100)
Vomiting	7 (25.9)	22 (33.8)
Neck stiffness	1 (3.7)	26 (40)
Mental change/ confusion/ psychological disorder	0 (0)	19 (29.2)

** Multiple responses present.

DISCUSSION

Powderley stated that cryptococcal and tubercular meningitis together account for about 3/4 of the cases of meningitis among HIV patients in western world.¹² But here in Indian continent we found that both comprised almost 100% cases. Among them most cases were cryptococcal meningitis (70.7%). Other variant of meningitis might be rare that we couldn't observe in one year study period or might be excluded from the study due to incomplete data. In North western Tanzania study among the laboratory confirmed cases 78.6% cases were cryptococcal meningitis and rest were Tubercular meningitis and their findings were collaborative with our study result.¹³

We found 51.9% HIV-TB meningitis patients in middle adulthood age (41-60 years). But Der et al found different age distribution among HIV-TB meningitis patients in Ghana study (only 38.6% belonged to 41-60 years group and 56.9% in 20-40 years age).¹⁴ Cryptococcal meningitis among HIV patients mainly confined among young adult age group (81.7%) that was also supported by Dash et al study finding (68.7%) conducted in Odisha, India. But its prevalence among young adult was higher than Dash et al study result.¹⁵ In our study we found (38.5%) more female cryptococcal meningitis patients compare to Dash et al study (25%).¹⁵ Mean CD4 cell count of HIV-TB meningitis patients of our study (143 cells/cumm) were found higher than Kumar et al study finding (96 cells/cumm).¹⁶ Similarly mean CD4 cell count of HIV-cryptococcal meningitis patients of our study (175 cells/cumm) were observed too high than Aslam et al study result conducted in Bengaluru (60 cells/cumm).¹⁷

In our study, mean CSF protein value of TB and cryptococcal meningitis patients (TBM=546.1 mg/dl, CCM=189.1 mg/dl) were not collaborative with Aslam et al (CCM=72.4 mg/dl) and Khan et al (TBM=289.48 mg/dl, CCM=432.18 mg/dl) study findings.^{17,18} Mean CSF glucose level of cryptococcal meningitis patients of our study (30.1 mg/dl) was found more or less same with Aslam et al (37.01 mg/dl) and Khan et al (32.63 mg/dl) study finding, but in case of TB meningitis our study finding (26.8 mg/dl) was not collaborative with Khan et al study result (52.32 mg/dl).^{17,18} Mean CSF cell count our study result (36 cells/cumm) was comparable with Aslam et al (21.11 cells/cumm) study result in case of cryptococcal meningitis but huge difference with Khan et al study result (529.54 cells/cumm).^{17,18} In case of TB meningitis our CSF cell count result (550 cells/cumm) was not collaborative with Khan et al study (228 cells/cumm).¹⁸

Headache, fever were found most predominant presenting features for both type of meningitis in different studies, but neck stiffness, mental change/ confusion/ psychological disorder were found in different proportion in different studies and their results were not comparable.¹⁵⁻¹⁸

From above discussion it can be assumed that TB and cryptococcal meningitis among HIV patients presented with different clinical and laboratorial features in different study settings. So further in depth prospective study is necessary in this field for better understanding of prognosis and characteristic of diseases.

CONCLUSION

This cross sectional study concluded that cryptococcal was common type of meningeal infection for HIV infected patients and mainly infected younger generation. CD4 count of the patient had no correlation with antigenicity of cryptococcal infection. TB and cryptococcal meningitis patients presented with different clinical and laboratorial features and these were also different from other study findings. In this field had very limited study. Our study provided a baseline data about epidemiology and clino-laboratorial features of HIV meningitis patients and will help for further investigation in this field.

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