CLINICAL AND LABORATORY PROFILE OF SIXTY PATIENTS WITH AIDS: A SOUTH INDIAN STUDY

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Abstract. Sixty patients who fulfilled the WHO case definition of acquired immunodeficiency syndrome (AIDS) were admitted and treated between January 1993 and June 1995 in JIPMER Hospital, Pondicherry, South India. Their mean age was 30.3 ± 6.4 years. Male : female ratio was 5 : 1. The heterosexual route was the major mode of transmission (96.7%). Fever was the commonest presentation (98.3%), followed by weight loss (85%) and cough (36.7%). The commonest opportunistic infection seen was tuberculosis (pulmonary, extrapulmonary - single or in combination) followed by esophageal candidiasis. Cryptococcal meningitis, intestinal crytosporidiosis, CNS toxoplasmosis, *Pneumocystis* pneumonia and group B *Salmonella* septicemia were the other infections encountered. Ten out of the 38 patients with tuberculosis were followed up on antituberculous treatment for 6 months. Seven out of 18 patients with esophageal candidiasis were treated with ketoconazole.

INTRODUCTION

Since the original description of the acquired immunodeficiency syndrome (AIDS), human immunodeficiency virus (HIV) infection has become recognised world wide and has now been reported from 173 countries (WHO, 1993). Although the majority of the *reported* cases of AIDS have occured in the countries of the western world, the greatest impact of HIV infection has been felt in the developing countries of subsaharan Africa and more recently in Asia.

The clinical profile of AIDS in India tends to be different from what is seen in the developed world, since the HIV infected individual in India lives in an environment with high prevalence of infectious diseases. The knowledge regarding the profile of patients of AIDS in this country is far from complete, and only a few reports are available. Tuberculosis may be the most important opportunistic infection in HIV-infected patients in India. Apart from tuberculosis, other presentations of AIDS in Indian patients that have been described include weight loss, chronic fever, chronic diarrhea, candidiasis, cryptococcal meningitis, cytomegalovirus retinitis, pneumocystis pneumonia and aspergillosis (Bollinger *et al*, 1995). We present the clinical profile of sixty patients of AIDS encountered in a span of two and a half years and the response of AIDS associated secondary infections to treatment.

MATERIALS AND METHODS

Patients who were admitted into the medical wards of JIPMER Hospital, between January 1993 and June 1995 were included in the study, if they fulfilled the following criteria:

i) Age more than or equal to 13 years

ii) Seropositive for HIV, by micro ELISA done twice, and positive by either an Immunocomb or HIV SPOT test.

iii) Fulfilment of WHO case definition for AIDS surveillance (WHO, 1986). For patients admitted after September 1994, the expanded WHO case definition for AIDS surveillance was used (WHO, 1994).

A predefined protocol was used to evaluate all patients. Investigations were based on clinical symptoms and signs.

Hemoglobin estimation, total leukocyte count, peripheral smear, platelet count, chest x-ray and ultrasonography of abdomen were performed on all patients. For patients with neurologic findings, CSF Gram stain and India ink preparation, CSF bacterial and fungal cultures and a CT scan were done. For patients with lymphadenopathy, fine

needle aspiration cytology (FNAC) of the node was performed, and if inconclusive, a biopsy of the node was done and histopathological examination and mycobacterial cultures were performed. Multiple cultures of urine, blood, sputum and stool were performed for febrile patients. Gram Stain, Ziehl Neelsen staining and bacterial cultures were performed on sputum of patients with respiratory symptoms or signs.

RESULTS

Out of 60 patients studied, 50 (83.3%) were males, and 10 (16.7%) were females, with a male : female ratio of 5 : 1. The mean age of patients was 30.3 ± 6.42 years (range 17 to 53, median 29 years). The maximum occurence was seen in the age group 21-30 years which comprised 60% of all the patients. Five percent of patients were below 20 years of age and another 5% were above 41 years.

The major mode of transmission was sexual. Out of the 50 male patients 49 were heterosexual and had multiple sex partners. There were no homosexuals. No risk factor could be identified in one male patient. Three out of the 10 female patients were housewives whose husbands were promiscuous, others were commercial sex workers. Blood transfusion was identified as a possible risk factor in one female patient.

History of fever was present in 59 out of 60 patients (98.3%). The second commonest symptom was weight loss found in 51 patients (85%), followed by cough in 22 patients (36.7%), vomiting in 19 patients (31.7%), odynopagia in 18 patients (30%) and diarrhea lasting for more than one month in 15 patients (25%). All the ten female patients had amenorrhea for more than 6 months.

The most common physical sign was pallor which was seen in 54 out of 60 patients (90%). Other physical signs included extreme emaciation in 39 (65%), lymphadenopathy in 33 (58%), oral thrush in 25 (41.75), hepatomegaly in 19 (31.7%), pleural effusion in 21 (20%), splenomegaly in 10 (16.7%) and genital ulcers in 11 (18.3%). Six patients (10%) had herpes zoster. Three patients (5%) had meningeal signs. The mean weight of the patients was 36.7 ± 6.62 kg (range 22 to 50 kg, median 36 kg).

Out of 60 patients, 54 (90%) had anemia, with a mean hemoglobin value of 8.83 ± 2.51 g% (range 4.4 g% - 15.5 g%, median 9.0 g%). In 53 out of 54 patients, peripheral smear showed normocytic normochormic RBCs. Hypochromic RBCs were found only in one patient. Thrombocytopenia (platelets less than 150,000/mm^3) was observed in three patients (5%), of which one had overt bleeding. Neutrophilia (absolute neutrophil count more than 7,000/mm^3) was a feature observed in 22 patients (37%). Lymphocytopenia (absolute lymphocyte count less than 500/mm^3) was noted in 15 patients (25%).

Nine patients (15%) had neurological manifestations, of whom two had cryptococcal meningitis (diagnosed by India ink preparation and culture), one had pyogenic meningitis (*Klebsiella* sp), one had a frontal lobe infarct (etiology not identified), one had focal seizures with normal CT scan (etiology not identified), one had proximal myopathy of hip girdle and one had peripheral neuropathy (demyelinating type). Two patients presented with hemiparesis and were diagnosed to have CNS toxoplasmosis presumptively by positive *Toxoplasma* serology and multiple ring enhancing lesions on CT scan.

Out of the 60 patients, 33 had lymphadenopathy. In all of them, the etiology was tuberculosis (diagnosed by FNAC/lymph node biopsy/myobacterial culture). The histologic picture was caseation necrosis or granulomatous lymphadenitis with acid fast bacilli (AFB). In most of the cases the population of AFB was quite dense. Cervical, axillary, epitrochlear, intrathoracic and intra-abdominal nodes were involved in various combinations. *M. tuberculosis* was isolated from the lymph node, by culture in one patient.

Ultrasonography of abdomen was performed in all the 60 patients and was found to be normal in 31 (51.7%). In the remaining 29 cases (48.3%) ultrasonography showed intra-abdominal lymphadenopathy, hypoechoic splenic shadows and hypoechoic hepatic lesions in various combinations.

Out of 33 patients with tuberculous lymphadenitis (Group I), 25 (75.7%) had abdominal involvement, while eight (24.3%) did not have abdominal involvement. Out of the 27 patients without tuberculous lymphadenitis (Group II), only four (14.8%) had abdominal involvement, while 23 (85.2%) did not have abdominal involvement. These

findings were significant statistically ($p < 0.0001$), (Table 1).

Out of the six patients with tuberculous lymphadenitis who died in hospital, two had hepatic hypoechoic lesions. Post mortem liver biopsies revealed tuberculosis. No invasive procedure was performed on the splenic lesions or on the intra-abdominal nodes in any of the patients.

Cardiopulmonary manifestations included pulmonary tuberculosis in 12 (diagnosed by sputum AFB staining), pleural effusion in five (due to *Pseudomonas aeruginosa* in one, *Mycobacterium tuberculosis* in four), bacterial lobar pneumonia (*Escherichia coli*) in one, pericardial effusion in two and constrictive pericarditis in one. A presumptive diagnosis of pneumocystis pneumonia was made in one patient who presented with dyspnea, cyanosis and bilateral hilar pneumonitis on chest x-ray; arterial blood gas analysis showed severe hypoxemia. Out of the 12 patients with pulmonary tuberculosis, seven had tuberculous lymphadenitis as well.

Extrapulmonary TB was the most common opportunistic infection (55%). Esophageal candidiasis (diagnosed presumptively if patient had oral thrush, scraping from which showed candida and odynophagia) was the second commonest infection (30%). The AIDS indicator disease diagnosed in our study are given in Table 2.

Other infections included herpes zoster in 6 (10%), extensive tinea corporis in five (8.3%), tropical pyomyositis in one, pyogenic menigitis in one, intestinal shigellosis in one and bacterial pneumonia in one.

Out of the 33 patients with tuberculous lymphadenitis only eight could be followed up. These patients were treated with INH, rifampicin, pyrazinamide and ethambutol for the first two months and with INH, rifampicin and ethambutol for the next four months. By the second month of treatment lymph nodes had completely disappeared in all patients. Only three patients completed six months of ATT. All lymph nodes (including abdominal nodes) in all the three patients and hypoechoic splenic lesions in two patients disappeared with treatment.

Nine out of 18 patients with esophageal candidiasis were administered ketoconazole. Seven patients were compliant to treatment, but odynophagia was relieved only in two patients. Two out of 12 patients with pulmonary tuberculosis who were followed up for six months showed complete improvement bacteriologically and radiologically. Out of the two patients of CNS toxoplasmosis who were treated, one expired while the other showed remarkable improvement with sulfadiazine and pyrimethamine. Both the patients of cryptococcal meningitis and the lone patient of cryptosporidial diarrhea died in hospital.

Table 1

Comparison of the ultrasound findings of patients with and without tuberculous lymphadenitis.

Group	Abdominal involvement	No abdominal involvement
I (n = 33)	25	8
II (n = 27)	4	23

Chi square = 22.09; $p < 0.0001$

Table 2

Indicator diseases of AIDS diagnosed in this study*

Indicator disease	No. of patients (n = 60)	Percentage
Extrapulmonary tuberculosis	33	55.00
Esophageal candidiasis	18	30.00
Pulmonary TB	12	20.00
HIV associated wasting+	7	11.70
Cryptococcal meningitis	2	3.33
Intestinal cryptosporidiosis	1	1.67
CNS toxoplasmosis	2	3.33
Pneumocystis pneumonia	1	1.67
Group B *Salmonella* septicemia	1	1.67

* Many patients had more than one indicator disease

\+ The term HIV associated wasting was applied only to those patients in whom no other secondary infection could be identified.

DISCUSSION

The Centers for Disease Control (CDC, Atlanta) case definition for AIDS is not practical in many

developing countries due to lack of sufficient investigatory backup. This leads to underestimation of the number of AIDS cases. Hence we have used the WHO cases definition for AIDS surveillance to define our cases. Limitations of this case definition are its relatively low sensitivity and specificity. Though the WHO case definition does not include HIV serology to diagnose AIDS, we have included HIV serology to diagnose our cases of AIDS. This probably has increased the specificity of diagnosis when compared to the WHO case definition. We have not used CD4 counts for diagnosis since this facility was not available at our hospital.

The male : female ratio in our study was 5:1. This is in sharp contrast to the ratio of 1:1 in Africa and 12:1 in the United States. The ratio of 5:1 observed in our study is probably because the male population at risk had sex with a much smaller population of female commercial sex workers (CSW), which is probably the most important mode of transmission. A similar ratio of 5:1 has been reported from a South Indian hospital (John *et al*, 1993). The vast majority of patients in the United States are homosexual or bisexual males. In contrast heterosexual transmission seems to be the dominant mode of transmission of HIV infection in Africa and other Asian countries.

Heterosexual transmission has been the predominant mode of transmission in our patients. Homosexualls and intravenous drug abusers are conspicuous by their absence in this study. This is comparable with data available from elsewhere in India, except in north eastern states of India where *iv* drug abuse is common (John *et al*, 1993).

The commonest hematological manifestation was anemia. In 53 out of 54 patients with anemia, the peripheral smear was normocytic and normochromic suggesting anemia of chronic disease. This is comparable with Western studies where 75-90% of patients with full blown AIDS have anemia of chronic disease (Glaspy *et al*, 1994). Thrombocytopenia was seen in 5% of our cases. This is much less than the 40% seen in Western studies (Abrams, 1988).

Tuberculosis was the most common secondary infection diagnosed in our study. Of the 38 patients with tuberculosis, 26 had tuberculous lymphadenitis alone, five had pulmonary tuberculosis alone and seven had both pulmonary tuberculosis and tuberculous lymphadenitis. Because of the high rate of dissemination of *M. tuberculosis* in AIDS, co-existence of pulmonary and extrapulmonary tuberculosis has been found in as high as 53% of patients with AIDS and tuberculosis in various prospective and retrospective studies (Pitchenik *et al*, 1988).

Abdominal involvement, either in the form of splenic hypoechoic lesions, hepatic hypoechoic lesions or abdominal lymphadenopathy has been a very usual finding in many of our cases of tuberculous lymphadenitis. Even though the exact etiology of these abdominal lesions are not clear, we presume that these finding are due to tuberculosis for the following reasons:

i) histology of peripheral lymph nodes seen in majority of these patients were suggestive of tuberculosis.

ii) post mortem biopsies performed in 2 patients with hepatic hypoechoic lesions were suggestive of tuberculosis.

iii) abdominal lymph nodes in 5 patients and splenic hypoechoic lesions in 3 patients disappeared with antituberculous treatment.

The second commonest secondary infection noted in our study group was esophageal candidiasis (30%). The diagnosis was presumptive if patients had odynophagia and oral swab showed fungal mycelia. We have not performed barium studies, upper gastrointestinal endoscopy or cytology of esophageal scraping to diagnose esophageal candidiasis. In a study of 27 patients of AIDS or ARC, by Raufman *et al* (1986), 16 had odynophagia, 2 had dysphagia, 3 had both symptoms and 6 had no symptoms of esophageal disease. Esophagoscopy was diagnostic of esophageal candidiasis in all 27 patients. Thus many patients with odynophagia or dysphagia and oral thrush had esophageal candidiasis. Many patients who did not have odynophagia or dysphagia also had esophageal candidiasis. If upper gastrointestinal endoscopy is done routinely for all patients with AIDS, the actual incidence of esophageal candidiasis can be determined and we presume that it will be much higher in our patients. Cryptococcal meningitis was diagnosed in two out 60 patients (3.3%). This is much less when compared to the occurrence of this infection in 6-12% of patients with AIDS in the United States. Cryptococcal meningitis was reported in 4 out of 61 patients from Vellore, South India (Sara *et al*, 1995).

One of our patients presented with frank meningitis and the other one with chronic headache.

CNS toxoplasmosis was diagnosed in two out of 60 patients. Reports of CNS toxoplasmosis has been rare from India. Four cases been reported from Bombay by Venkatachalam *et al* (1995).

Intestinal cryptosporidiosis was diagnosed in only one out of 60 patients (1.7%). This is in contrast to the finding of intestinal cryptosporidiosis in 50% of patients with AIDS in Haiti and Africa (Quinn *et al*, 1986).

Group B *Salmonella* septicemia was diagnosed in one of our patients with fever. He was lost to follow up.

HIV wasting syndrome is the most common mode of presentation of AIDS in Africa (Fleming, 1990). 51 out of 60 of our patients had weight loss. In 7 of these patients no cause for wasting was identified and therefore we have classified them under HIV associated wasting.

The AIDS defining indicator diseases diagnosed in our study were different from the scenario prevailing in western countries. In a study of clinical and autopsy features of 250 AIDS patients from Milan, Italy, it was seen that the most frequent clinical diagnosis were *Pneumocystis* pneumonia, and esophageal candidiasis. Forty-seven % of the disease found at autopsy had not been diagnosed during life; CMV infection, mycoses, HIV specific brain lesions, cerebral lymphomas, and progressive multifocal leukoencephalopathy (PML) had a higher rate of non diagnosis during life (d'Arminio Monoforte *et al*, 1992). These findings are in contrast to the findings in our study in which tuberculosis was the commonest opportunistic infection. Compared to the profile of studies reported from the US also, tuberculosis and esophageal candidiasis were more frequent in our study.

Table 3 compares the AIDS defining diseases observed in our study with those reported from Christian Medical College, Vellore, South India.

Table 3

Comparison of AIDS associated infections observed in this study with those observed at Vellore, southern India.

Diagnosis	Present study (n = 60) (Jan 1993 to June 1995)		Sera *et al* (1995) CMC, Vellore India (n = 61) (Feb 1986 to June 1992)	
Pulmonary TB alone	5	(8.3%)	10	(16.6%)
Pulmonary and extrapulmonary TB	7	(11.67%)	15	(24.9%)
Only extrapulmonary TB	26	(43.3%)	7	(11.67%)
Tuberculosis (overall)	38	(63.3%)	32	(52%)
Oropharyngeal candidiasis	18	(30%)	25	(41%)
Cryptococcal meningitis	2	(3.3%)	4	(7%)
Cryptosporidial diarrhea	1	(1.67%)	4	(7%)
CNS toxoplasmosis	2	(3.3%)	0	(0.00%)
Group B *Salmonella* septicemia	1	(1.67%)	3	(4.90%)
CMV retinitis	0	(0.00%)	2	(3.3%)
Pneumocystis pneumonia	1	(1.67%)	0	(0.00%)
Interstitial pneumonitis	0	(0.00%)	2	(3.33%)
Recurrent zoster	0	(0.00%)	1	(1.67%)
Oral hairy leukoplakia	0	(0.00%)	1	(1.67%)
Kaposi's sarcoma	0	(0.00%)	0	(0.00%)
Immunoblastic lymphoma	0	(0.00%)	1	(1.67%)

Outcome

All patients with rare secondary infections, such as cryptococcal meningitis, cryptosporidiosis, pneumocystis pneumonia and one patient of CNS toxoplasmosis expired. The patient with presumptive pneumocystis pneumonia presented with severe illness and could not be salvaged even though cotrimoxazole and steroids were instituted. One patient with CNS toxoplasmosis however responded to a combination of pyrimethamine and sulfadiazine and is presently on follow up.

Out of the eight patients of tuberculous lymphadenitis who were followed up, seven responded completely to treatment. Two of them later died of cryptococcal meningitis. Our findings suggest that AIDS associated tuberculous lymphadenitis responds well to antituberculosis treatment.

Esophageal candidiasis on the other hand was a difficult condition to eradicate. Out of the seven patients who were put on ketoconazole only two patients were relieved of their symptoms seven though oral thrush had disappeared in all. The poor response could be due to gastric achlorhydria, which might have affected the absorption of ketoconazole, or due to development of resistance to ketoconazole.

Our study has highlighted many interesting features of AIDS in Indian patients. Many unresolved questions can be answered only if sophisticated and expensive immuno - cytological studies and autopsies are performed in these patients, which may unveil the complete spectrum of AIDS in Indian context.

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