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THE CLINICAL PROFILE OF HIV INFECTED PATIENTS OF TEACHING HOSPITAL IN PUNJAB AND THE RELATION WITH ABSOLUTE CD\textsubscript{4} AND CD\textsubscript{8} COUNTS

SINGH R*, ARORA D **, KAUR M ***, KUMAR R****

ABSTRACT

The most common cause of HIV disease throughout the world is HIV-1 which was first identified in West Africa. Worldwide, the World Health Organization (WHO) estimated that there were 1 million HIV-1 infected people in South America, 0.5 million in Europe, 5 to 6 million in sub-Sahara Africa, and 30,000 in Oceania. In spite of it being highly prevalent in the world there have not been many studies to study its clinicopathological behavior in this part of the world. Hence the present study was planned to study the clinical profile of HIV positive patients presenting to a tertiary care hospital, absolute CD\textsubscript{4} and CD\textsubscript{8} cell count in HIV positive patients at the time of presentation and the association of CD\textsubscript{4} and CD\textsubscript{8} cell counts with the predominant clinical infection at the time of presentation.

* (Asst. Prof.), Dept of Medicine, ** (Asst. Prof.), Dept of Microbiology, ***(Asst. Prof.) Dept. of Radiodiagnosis, **** (Lecturer) Dept. of Microbiology, Adesh Medical college and Hospital, Bhatinda, Punjab-151001. (India)

Corresponding Author:
Dr. Deepak Arora (Asst. Prof.)
Dept. of Microbiology
Adesh Medical college and Hospital.
Bhatinda, Punjab, India-151001.
E-mail: drdeepakarora@yahoo.co.in
Tel: +91-9781566786. Fax: +91-0164 2742902

Introduction

The most common cause of HIV disease throughout the world is HIV-1 which was first identified in West Africa. Since the first cases of AIDS were reported in 1981, more than 179,000 cases of AIDS have been reported in the United States and 1,13,000 (63%) of these patients have died. This disease is now a leading cause of death among men and women under 45 years old and of children under 5.

Worldwide, the World Health Organization (WHO) estimated that there were 1 million HIV-1 infected people in South America, 0.5 million in Europe, 5 to 6 million in sub-Sahara Africa, and 30,000 in Oceania. In 1992 the emergence and recognition of HIV-1 infection in Thailand and India – where WHO estimated that 1 million people were infected – was an ominous although predictable development. In addition to the large number of already infected individuals, there is the potential for rapid spread into an enormous population of susceptible people. Maternal – infant transmission reportedly occurs in between 7% and 39% of infected mothers [1]. It may be due to transplacental infection. Infection could also occur at birth (virus may be present in cervical secretions) or rarely from maternal milk [2].

Indian Scenario

HIV infection in India was detected in a group of commercial sex workers in Chennai in Tamil Nadu in 1986. Initially the disease was located to three epicenters namely Manipur, Maharashtra and Tamilnadu, but since then it is a rapidly evolving epidemic in most parts of the country. According to
the analysis of the recent rounds of sentinel surveillance conducted in October 1999, the HIV prevalence in the adult population can be broadly classified into 3 groups of States/Union territories in the country.

**Group I:** Generalized epidemic: where the HIV infection has crossed 1% or more in antenatal women. The states included in this group are Maharashtra, Tamilnadu, Karnataka, Andhra Pradesh and Manipur.

**Group II:** Concentrated epidemic: includes those states where the HIV infection is <1% in the antenatal women but has crossed 5% or more among the high risk groups. These states are Gujarat, Goa, Kerala, West Bengal and Nagaland.

**Group III:** Low-level epidemic: include the remaining states where the HIV infection in any of the high-risk group is still less than 5% and <1% among antenatal women.

**Materials And Methods**

The present study was conducted in the department of Medicine, Adesh Institute of Medical Sciences & Research, Bathinda. The study was performed over a period of two years from May 2006 to May 2008. All the HIV positive patients who presented to the hospital and susceptible family members of the HIV positive patients were screened and if found symptomatic and seropositive were included in the study.

All the suspected patients were screened by ELISA technique using EIA Kit provided by Ortho diagnostics. Assayed on AMP (Automatic Microplate Processor), fully automatic EIA reader from Johnson and Johnson. 2ml blood sample was collected under aseptic technique for the same and assayed for HIV status. Cut off values for labeling HIV patients more than or equal to 0.250 absorbance value – HIV positive patient less than 0.250 absorbance value – HIV negative patient.

If positive further consecutive tests which were done were:

(a) Dot immunoassay for detection of antibody to HIV1&HIV2 (COOMBS).
(b) HIV tri-dot test designed using gp41 & gp36 representing the immunodominant region of HIV1&2.

Even if a patient was HIV positive previously we included him in the study. Also spouses of the patients were examined wherever possible (if consent given) and incorporated into the study.

After confirmation of HIV positivity, samples of whole blood were sent for CD4 and CD8 counts. This investigation was carried out by an accredited laboratory. With fully aseptic technique, 3 ml whole blood was collected in both EDTA and heparin; vacuettees and samples were sent to the collection center on the same day. The samples were processed by flow cytometry for CD4 and CD8 cell count.

On the basis of the clinical picture and the CD4 and CD8 cell counts the subjects were divided into categories as shown in table7.5

The data collected on various variables were subjected to statistical analysis. Mean and standard deviations were computed. To compare the outcome of two groups, Fisher’s Z test and Chi square tests were applied. Karl Pearson’s coefficient was also applied to see the relationship between two variables.

**Results And Observations**

1. **Age And Sex Distribution**

Disease is affecting mainly the people in sexually active age group 15-44 years. Out of the total 50 patients who met the inclusion criteria; there were 36 (72%) males and 14 (28%) females. The age range varied from 3½ years to 60 years, amongst the males, with the mean being 39.46±12.38 years. The maximum incidence (decade wise) was seen in the age range of 31-40 years. In the females the age range varied
from 7 to 60 years with the mean age being 38.50±14.81 years [Table/Fig 1].

2. Occupation Wise Distribution
Out of 50 patients, 9 (18%) were agriculturists, 5(10%) were truck driver, 5(10%) were laborers, 4(8%) were policemen, 3(6%) were government employees, 2(4%) were school teachers, 2(4%) were representing the armed forces, 2(4%) were in private job and 3(6%) were students. Out of these 3 students 2 were males and one was female. There was one child aged less than 5 years, who was HIV positive and his parents and sibling were also HIV positive. There was one businessman. Apart from one female student all the other 13 females (26%) were housewives [Table/Fig 2]

3. Mode Of Spread
The maximum incidence was through exposure to commercial sex workers (42%), parenteral injections (28%), and unprotected sex with spouse (16%).4% was vertical transmission from mother to child while transmission could not be ascertained in 10% of the subjects [Table/Fig 3].

4. Symptomatology And Its Analysis
The most common symptoms observed in the study group were fever, cough, anorexia, diarrhea, headache and fatigue as shown above. Fever was the most common symptom seen in 30(60%) patients. Out of these 30 patients, 24 were males (66.66%) and 6 were females (42.85%). Cough was seen in 11 (22%) patients [Table/Fig 4].
Dual Infections

Dual infection was said to exist when a HIV positive patient had evidence of another infectious disease. The common infections noticed in the study group [Table/Fig 5].

5. Dual Infections

Oral Candidiasis

The most common dual infection in the study group was oral candidiasis. It was identified by examination of the oral cavity using a well lit torch. It was primarily a clinical diagnosis. It was found to exist in 23 (46%) patients at the time of presentation.

Tuberculosis

The second most common dual infection in the study group was Tuberculosis which was diagnosed in 12 (24%) patients. The diagnosis was based on radiographic evidence, Fine Needle Aspiration Cytology (FNAC), Ultrasonography (USG). Analysis of Cerebro Spinal Fluid (CSF), Ascitic and pleural fluid examination and sputum AFB wherever applicable were done but none of the patients had sputum smears positive for mycobacterium. Six had abnormal chest X-rays suggestive of pulmonary tuberculosis.

Pneumonia

The third most common dual infection in the study group was pneumonia. It was present in 10 (20%) patients. The diagnosis was based on chest radiographs and clinical features [Table/Fig 6].

Cryptococcosis

In the study group there were 2 (4%) patients who presented with cryptococcal infection. One patient was male and the other was female. Both these patients presented with symptoms of headache, fever and vomiting. Neck stiffness was present in both and one of them was in altered sensorium. C.S.F. was positive for cryptococcal antigen in both the patients. In one patient the CSF showed on Indian Ink Preparation many capsulated budding yeast cells, the morphology of which was suggestive of *Cryptococcus neoformans*. Gram’s staining showed - gram positive capsulated budding yeast cells.
Brain Abscess
2 (4%) patients presented with brain abscess. Both were males. One patient presented with fever, hemoptysis and altered sensorium. The CT scan of the head showed a space occupying lesion. MRI of the head showed large well defined ring enhancing focal lesion. Abscess drainage was done. The tissue sent for histology examination showed a few gram positive cocci. Abundant pus cells were seen. Tissue was negative for AFB and Culture. No granuloma / tumor cells were seen [Table/Fig 7].

The patients were categorized according to their CD4 cell count [Table/Fig 8]. In the study group the highest CD4 cell count was 726, the lowest CD4 cell count was 05 while the average CD4 count was 114.7. The highest CD4 cell count was 2578, the lowest CD4 cell count was 54 and the average CD8 count was 501.5.

6. CD4 Counts In Relation To Candidiasis
23 patients who had candidiasis were categorized according to the CD4 counts into A, B & C categories [Table/Fig 8]. The comparison between group B v/s C revealed no significant difference [Table/Fig 9].

7. CD4 Count In Relation To Tuberculosis
In study group there were 12 patients who had tuberculosis. Out of 12, 10 were males and 2 were females. The patients had been categorized according to CD4 counts into A, B & C categories as shown in the table. The comparison between group B v/s C revealed no significant difference [Table/Fig 10].
8. Clinical Categories According To CD4 / CD8 Ratio And Its Correlation With CD4 Counts

Normal CD4/CD8 ratio varies from 0.6 – 2.8. In the study group, 5 patients had CD4/CD8 count ratio ≥0.50. 21 patients had CD4/CD8 count ratio between 0.2-0.49. 24 patients had CD4/CD8 count ratio < 0.20. The CD4 average / CD8 average ratio was = 0.228 [Table/Fig 10]. There was a significant positive correlation between CD4 and CD4/CD8 ratio for the patients who had candidiasis, tuberculosis & cryptococcal meningitis and for the study group as a whole, however for the patients with tuberculosis the correlation coefficient was observed to be negative.

Discussion

The present study was conducted in the Department of Medicine at Adesh Institute of Medical Sciences & Research, Bathinda, with an aim to evaluate the clinical profile, the absolute CD4 and CD8 counts of HIV infected patients presenting to a teaching hospital in Punjab. All HIV positive individuals who met the inclusion criteria were included. Detailed history, clinical examination and investigative work up were done. The epidemiological analysis of the case data shows that the disease is affecting mainly the people in the sexually active age group of 15-44 years. In the present study the age range varied from 3½ years to 60 years. The maximum incidence (decade wise) was seen in the age range of 31-40 years. In the females the age range varied from 7 years to 60 years with the mean age being 38.50±14.81 years. The maximum incidence (decade wise) was seen in the age range of 21-30 years. Hence female patients were involved at younger age group which is almost consistent with the NACO analysis.

Over the years HIV infection has increased sharply among commercial sex workers, rapidly increasing among STD clinic attendants and steadily progressing among low risk population. The present study has shown that now HIV infection is not only limited to commercial sex workers and truck drivers, but it has spread to the agriculturists, laborers and other low risk population. Interestingly no commercial sex worker was seen in the study group. The reason could be the social taboo associated with the labeling of commercial sex worker.

Epidemiological analysis of the AIDS by NACO, 2003 (India) showed that maximum transmission is through heterosexual contact, (85.27%), through blood and blood products (2.69%), through injection drug users (2.35%) and the history was not available in 7.01%. In a study by Patricia M. Spittal et al [4] HIV incidence rates among female injection drug users in Vancouver are about 40% higher than those of male injection drug users. In the present study the maximum incidence was through exposure to commercial sex workers (34%), parenteral injections (26%), & unprotected sex with spouse (16%). The mode of transmission could not be ascertained in 10% of the subjects. Mother to fetus transmission occurred in 4% of the patients. The reason is not far to seek. Most of the individuals in this part of the country are addicted to multiple substances. Hence the disparity

In a study by Danai Kitkungvan et al,[5] most common infectious etiologies of pyrexia of unknown origin were Mycobacterium tuberculosis (n = 30; 42%), Cryptococcus neoformans (n = 17; 24%), Pneumocystis jiroveci (n = 9; 13%), Toxoplasma gondii (n = 5; 7%), and salmonella bacteraemia (n = 5; 7%). Nineteen patients (26%) had co-infection with two or more pathogens. Similarly in our study tuberculosis is the most common infectious agent followed by Cryptococcosis.

Levine SJ and White DA [6] observed that Pneumocystis Carinii Pneumonia can present with fever in 79-100%, cough in 59-
91%, dyspnea in 29-95% and chest pain in 14-23%. Kovacs JA, et al [7] observed that HIV patients usually present with the usual symptoms but have a more insidious course as compared with other immuno compromised patients.

In the present study fever was the most common symptom seen in 30(60%) patients. Out of these 30 patients, 24 were males (66.66%) and 6 were females (42.85%). Cough was seen in 11 (22%) patients. Out of these 11 patients 9 were males (25%), 2 were females (14.28%). Dyspnea was present in 5 (10%) of the patient, out of these patients 3 were males (6%) 2 were females (4%).

Zuger A, et al [8] observed that meningitis was the most common initial manifestation affecting 72% to 90% of patients with cryptococcosis. Fever and headache were the most common symptoms occurring in about 65% to 90% patients. Less common manifestations were photophobia and neck stiffness 30% and an alternation of mental status 20%. Focal neurological deficits and seizures are unusual (<10%) and may reflect the presence of a second HIV – related illness. In the current study fever was present in 60% of the patients, headache in 12% of the patients, encephalopathy in 8% and seizures were observed in 4% of the patients.

Greenspan D [9] noted that candidiasis was the most common fungal infection observed in HIV infected patients. Candidiasis of the mucous membranes occurred in greater than 90% of patients at some point in their illness. In our study the most common dual infection was oral candidiasis. It was found to exist in 46% patients at the time of presentation.

Beck-Sague C, et al [10] observed that HIV infection increased the susceptibility to both primary and reactivation tuberculosis. A tuberculosis outbreak in a residential facility for HIV infected persons documented that early progression of new infection may occur in almost 40% of exposed HIV infected persons compared with approximately 5% of historical, non HIV-infected controls.

Selwyn PA, et al [11] in a prospective study of intravenous drug users found that tuberculosis in HIV infected persons most frequently resulted from reactivation of latent infection. Among individuals who previously had a positive response to tuberculin skin testing with purified protein derivative (PPD) and did not receive prophylaxis, the number of cases of tuberculosis per 100 person years was 7.9 in the HIV positive group compared with 0 in the HIV negative group.

In the present study the second most common dual infection was Tuberculosis which was diagnosed in 12(24%) patients. The diagnosis was based on radiographic evidence, Fine Needle Aspiration Cytology (FNAC), analysis of Cerebro Spinal Fluid (CSF), Ascitic and pleural fluid examination, USG (Ultrasoundography) and sputum AFB wherever applicable were done but none of the patients had sputum smears positive for mycobacteria.

Kovacs JA, et al [7] reported that early in the AIDS epidemic, approximately 75% of HIV – infected patients suffered at least one episode of PCP and it was often recurrent. Because of the widespread use of primary and secondary prophylaxis, the incidence of PCP has decreased since 1988. A prospective longitudinal study of the natural history of HIV infection in approximately 5000 homosexual men in the United States (multi – center AIDS cohort [MAC]study) found that PCP as an AIDS defining illness decreased from 47% in 1988 to 25%.

Hirschtick R, et al [12] studied the risk factors for development of bacterial pneumonia and identified low CD4 counts, cigarette smoking, intra venous drug use, and possible neutropenia as risk factors.

In the present study the third most common dual infection was pneumonia. It was
present in 10 (20%) patients. The diagnosis was based on chest radiography and clinical features. Most of them had a lower CD$_4$ counts, and many had addictions including smoking.

**Dismukes WE** [13] stated that cryptococcal meningitis was the most common central nervous system fungal infection in HIV-infected patients in the United States. **Clark RA et al** [14] observed that the presenting clinical features of cryptococcal meningitis were often subtle and nonspecific and included malaise, fever, nausea, vomiting, and head ache in 75% to 90% of the patients.

In the present study there were 2(4%) patients who presented with cryptococcal infection. Both of these patients presented with symptoms of headache, fever and vomiting. Neck stiffness was seen in both patients and one patient was in altered sensorium. CSF was positive for cryptococcal antigen in both the patients. In one patient the CSF showed on Indian Ink Preparation many capsulated budding yeast cells.

**Perkocha LA, Rodgers GM** [15] noted that the most frequent form of anaemia in AIDS had the characteristics of anaemia of chronic disease. The mean hemoglobin levels of patients with AIDS were reported to be between 9 and 10 gm/dL. **Sloand EM, et al** [2] in a retrospective study of 1004 patients attending an out patient HIV clinic found thrombocytopenia in 21% of patients with symptomatic AIDS and 9% of asymptomatic HIV — seropositive patients. Thrombocytopenia was correlated to low CD$_4$ lymphocyte counts and older age.

In the present study majority of the patients presented with anaemia. The most common form of anaemia was anaemia of chronic disease. 86% of the male patients had anaemia and 50% of the female patients had anaemia. 19.44% males had thrombocytopenia and 7.4% of females had thrombocytopenia. Most patients with thrombocytopenia had lower CD$_4$ counts.

**Stephen J. Mcphee Maxine A. Papadakis** [16] studied the relationship of CD$_4$ counts to development of opportunistic infections. When the CD$_4$ counts > 500/µL the following opportunistic infection were found to occur: Bacterial infections, tuberculosis, herpes simplex, herpes zoster, vaginal candidiasis, hairy leukoplakia, Kaposi’s sarcoma. When the CD$_4$ counts vary between 200-499/µL, opportunistic infections were reported eg. pneumocystosis, toxoplasmosis, cryptococcosis, coccidioidomycosis, cryptosporidiosis. When the CD$_4$ counts <50/µL, opportunistic infections reported were disseminated MAC infection, histoplasmosis, CMV retinitis and CNS lymphoma most of the Indian studies including one by **Sengupta et al** [17], [18] showed oral candidiasis to be the predominant oral lesion present in about 36% of the patients.

In the present study out of 50 patients, one patient had ≥ 500 / µL CD4 counts. Eight patients had a CD$_4$ count between 200-499/µL. Out of these 8 patients, 4 had candidiasis, 2 had tuberculosis, 2 had pneumonia and 1 had brain abscess. The remaining 41 patients had CD$_4$ count < 200/µL. Out of these 41 patients 19 had candidiasis, 10 had tuberculosis, 8 had pneumonia, 2 had cryptococcal infection and 1 had brain abscess.

**Summary And Conclusions**

The present study was designed and conducted to know the clinical profile, the absolute CD$_4$ and CD$_8$ counts of HIV infected patients presenting to a teaching hospital in Punjab. All the HIV positive patients presented to the Hospital and susceptible family members of the HIV positive patients were screened and if seropositive and symptomatic were included in the study. The age and sex distribution, occupation, symptomatology, opportunistic infections and their relation to absolute CD$_4$...
cell counts and CD$_4$/CD$_8$ ratio has been assessed.

The epidemiological analysis of the AIDS case data shows that:

- Disease is affecting mainly the people in sexually active age group 15-44 years.
- The predominant mode of transmission of infection in the AIDS patients is through heterosexual contact (58%), through exposure to commercial sex workers (42%), followed by parenteral injections (28%). A higher incidence of parenteral drug users in this part of the country resulted in more number of patients with H.I.V. in injection drug users.
- Males account for 72% of AIDS cases and females 28%. The ratio being 3:1.
- The major opportunistic infection in AIDS patients is tuberculosis indicating a dual epidemic of tuberculosis and HIV.
- HIV in the present scenario is not restricted to any particular occupation as evidenced from our study. This probably tries to break the myth that truck drivers and those from the defence forces are the ones predominantly associated with HIV. Most of the females however get infected through unprotected intercourse with their husbands.
- Fever, cough decreased appetite diarrhea and headache were the chief clinical symptoms. Other common symptoms were breathlessness, weight loss, nausea / vomiting, altered sensorium, oral ulcers, abdominal pain, malena and swelling over feet.
- The most common infection was oral candidiasis seen in 23%(46%) of patients, followed by tuberculosis. Other infectious pulmonary diseases include bacterial mycobacterial, fungal and viral pneumonia's. Tuberculosis occurs more commonly in both in developed and developing countries. Since mycobacterium tuberculosis is a more virulent organism then P. carinii, tuberculosis often occur early in HIV infection and prior to the diagnosis of AIDS. It can also occur at the concomitant with or after that diagnosis.
- Out of 50 patients only 1 patient had CD4 counts > 500 /µL. most of the patients had relatively low CD4 counts (< 200/µL). The highest CD4 count was 726/µL while the lowest count was 5/µL.
- Community acquired pneumonia in the settings of HIV infections often occurs prior to the diagnosis of AIDS and the most common causative organism and pneumococcus and haemophilus influenza.

Hence it is concluded that the clinical profile of the patients with HIV positivity in a developing country differs in many ways from that of developed ones. The important ones being most of the patients acquire their infection through heterosexual routes. More so from commercial sex workers. Also since tuberculosis is so rampant in the Indian setting this was the chief infection in the patients.

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