ORIGINAL ARTICLE

JIACM 2019; 20(1): 43-46

Clinico-Immunological Correlation Among HIV-Infected Persons in North-Western India

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Abstract

Background: Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency syndrome (AIDS) were identified more than 38 years ago and have been associated with significant morbidity and mortality.

Aims and objectives: To stage, clinically and immunologically, the HIV-infected patients presenting to a tertiary care centre in North-western India.

Materials and methods: This was an observational cross-sectional study done by the department of medicine from 1st October 2014 till 31st March 2016 on HIV-infected individuals above 15 years of age. The diagnosis of HIV was made by using 4th generation ELISA kit. All patients were then clinically and immunologically staged as per WHO guidelines.

Results and conclusions: Amongst a total of 102 patients, 76 (74.51%) were males; 71 (69.60%) patients had age between 26 - 55 years. Majority of the patients, i.e., 84 (82.35%) were symptomatic on presentation. Constitutional symptoms were the commonest seen in 49 (48.03%) patients. There were 42 (41.18%) patients in WHO clinical stage 4 and severe immunosuppression was present in 60 (58.88%) patients with 54 (90%) patients in WHO clinical stage 3 and 4. Gastrointestinal opportunistic infections were the commonest.

Key words: HIV, AIDS, immunosuppression, opportunistic infections.

Introduction

Human Immunodeficiency Virus (HIV) infection and Acquired Immunodeficiency Syndrome (AIDS) have been challenging humanity for more than thirty eight years now and have been a significant public health concern worldwide[1]. Globally, roughly 36.9 million people are having HIV[2]. The majority of new HIV infections are from developing countries. Some important factors contributing to the increased impact of HIV in these countries are poverty, social stigma, and barriers to testing and treatment of HIV[4]. According to the National AIDS Control Organisation (NACO), 20.9 lakh people are suffering from HIV/AIDS in India. Estimated prevalence of HIV amongst adults in India is 0.26%[5]. The state of Punjab has around 31,961 estimated cases of adult patients with HIV[6].

The clinical behaviour of the patients with HIV is very different in different countries. In India, opportunistic infections like tuberculosis, cryptococcal meningitis, papular eruptions, and cytomegalovirus retinitis are common[7]. The clinical presentation of these patients to tertiary care is varied. They could either be incidentally detected or could be presenting with various opportunistic infections.

In the setting of limited resources in the developing countries, doing viral load for all patients may not be possible. So, in these areas, clinical judgement based on the patient's disease status may be valuable. For this, the World Health Organisation (WHO) has laid down specific criteria for HIV surveillance, clinical staging, and immunological staging. This is based on clinical features and not on laboratory parameters[8].

Clinical staging can be helpful where CD4 or other laboratory investigations are not available. However, CD4 testing may help us in determining the degree of immunocompromise, and would be useful in clinical decision-making[8].

In an earlier study from Eastern India, it was noted that a majority of the patients presented to the hospital in the WHO clinical stage 3 or 4, and 80 - 83% were initiated on anti-retroviral therapy at the time of presentation[9].

The present study has been undertaken to find out the level of immunosuppression amongst the patients presenting to our hospital by staging them clinically and immunologically. This would aid in HIV surveillance and would guide clinicians in their further treatment plan.

Aims and objectives

To clinically and immunologically stage all patients with HIV infection.

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Material and methods

This was an observational cross-sectional study done by the Department of Medicine at Christian Medical College and Hospital, Ludhiana, from 1st October 2014 to 31st March 2016.

Inclusion criteria

All diagnosed HIV-infected individuals above the age of 15 years, who presented to the Christian Medical College, Ludhiana, were included after taking an informed consent.

Exclusion criteria

1. Blood donors who were detected to be HIV positive.
2. Patients who were not willing to give consent.

Diagnosis: The diagnosis of HIV was made by 4th generation ELISA kit (J. Mitra) which has a sensitivity of 100% and specificity of 99.95%. The standard NACO protocol for confirmation of HIV was used.

After an informed consent from the patient, (or from legally acceptable relative of a minor or a patient in altered sensorium), demographic data, history, and detailed clinical examination was conducted. Investigations sent included a complete blood count, renal function test, CD4 count, and chest X-ray. Further investigations were based on the clinical features of the patients. The findings were noted in the protocol.

All the patients were clinically and immunologically staged as per the WHO guidelines. The patients were treated for opportunistic infections as required. All patients were initiated on antiretroviral therapy (ART) as per guidelines. Treatment was continued for those who were already on ART.

Statistical analysis

Number and percentage (%) were used for categorical variables and mean ± SD and median were used for continuous variables. Chi-Square test/Fisher's exact test were used for qualitative variables. Independent T-test/Mann Whitney test (for non parametric data) were used to compare quantitative variables. The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

Results and analysis

A total of 102 cases of HIV were registered in the study, out of which 94 (92.6%) were from Punjab. There were 76 (74.51%) males and 26 (25.49%) females. Majority of these patients, i.e., 71 (69.60%) were between 26 - 55 years of age. The age range included 16 - 75 years with mean age of 45 years. There were 81 (79.41%) patients who were married and staying with their spouses and 12 (11.6%) patients were unmarried.

There were 55 (53.92%) patients diagnosed to have HIV for at least six months before presentation, 31 of who were diagnosed on admission to the hospital. There were 10 patients who were diagnosed to be HIV positive for more than 10 years. The mean time to diagnosis of HIV was 26.4 months. There were 84 (82.35%) patients who were symptomatic at presentation, 60 (71.42%) of whom were people living with HIV (PLHIV).

Constitutional symptoms were present in 49 (48.03%) patients, with fever being the commonest presentation in 35 patients, followed by gastrointestinal symptoms, in 44 (43.13%) patients.

Amongst the opportunistic infections at the presentation, pulmonary infections were present in 22 patients, with tuberculosis being diagnosed in 14 patients and *Pneumocystis Jirovecii* pneumonia in 6 patients (Table I). Oral candidiasis was present in 17 patients and diarrhoea due to *Cryptosporidium* was diagnosed in 9 patients. The spectrum of neurological involvement included cryptococcal meningitis, tubercular meningitis, CNS toxoplasmosis and PMLE. Disseminated tuberculosis was present in 3 patients. There were 3 patients presenting with 4 or more opportunistic infections.

Amongst the 102 patients with HIV, 60 (58.88%) patients had a CD4 cell count of less than 200 cells/µl indicating severe immunosuppression; 28 (27.45%) had CD4 count between 200 - 349 cells/µl indicating advanced immunosuppression; 7 (6.86%) patients had CD4 count in the range of 350 - 499 cells/µl indicating mild immunosuppression and 7 (6.86%) patients had a CD4 cell count of more than or equal to 500 cells/µl indicating no

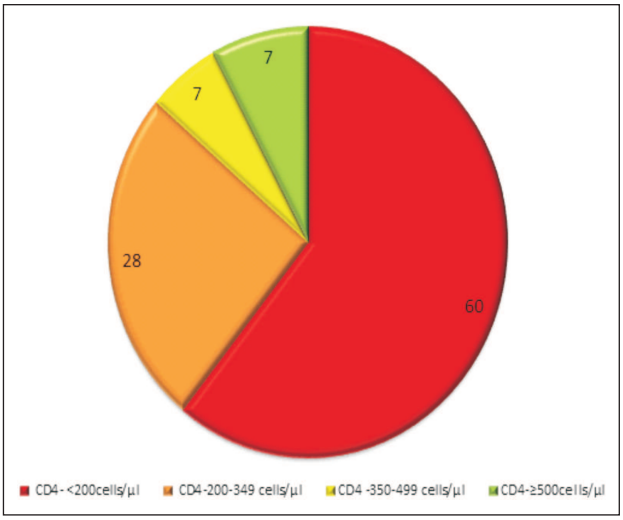

Fig. 1: *Immunological stage.*

significant immunosuppression (Fig.1).The mean CD4 count was 195 cells/µl with the lowest CD4 count being 2 cells/µl and the highest being 1,072 cells/µl.The patient with CD4 count of 2 cells/µl was diagnosed to have tuberculosis, cryptosporidiosis and klebsiella pneumonia, whereas the one patient with CD4 count of 1,072 cells/µl was asymptomatic and was tested for HIV, when admitted for drug de-addiction.

Table I: Spectrum of opportunistic infections.

Spectrum	n = 102	
Dermatological	**3 (2.94%)**	
Herpes genitalis		1
Molluscum contagiosum		2
Gastrointestinal tract	**34 (33.33%)**	
Oral candidiasis		17
Cryptosporidia		9
Cyclospora		7
Candida oesophagitis		3
CMV oesophagitis		1
HSV ulcers-oesophagus		1
Isospora		3
Abdominal tuberculosis		1
Respiratory system	**22 (21.56%)**	
Miliary tuberculosis		6
Candidiasis of the respiratory tract		2
PJ Pneumonia		6
Pulmonary tuberculosis other than miliary		8
CNS	**11 (10.78%)**	
Cryptococcal meningitis		5
CNS toxoplasmosis		2
PMLE		2
Tubercular meningitis		3
Other systems	**9 (8.82%)**	
Bone marrow TB granuloma		3
Splenic tubercular nodules		1
Tubercular lymphadenitis		5

Amongst the 102 patients diagnosed with HIV, there were 42 (41.18%) patients in WHO clinical stage 4 and 32 (31.37%) patients in WHO clinical stage 3 giving a total of 74 (72.55%) patients (Table II) who were in advanced WHO clinical stage, at the time of enrolment in the study (Fig. 2).

However, all patients with advanced and severe immunosuppression (CD4 < 350/µl) had opportunistic infections. In those with severe immunosuppression, GI infections were present in 28 (46.66%), followed by

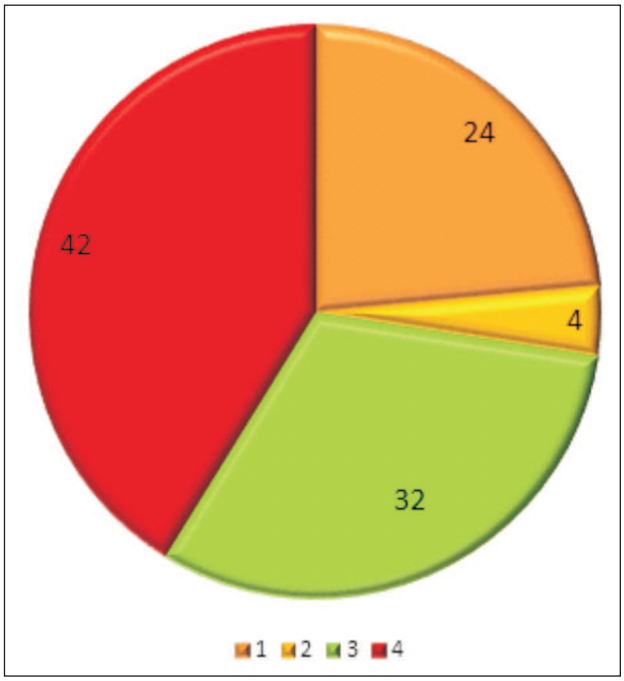

Fig. 2: *WHO clinical stage.*

respiratory in 21 (35%) and CNS infections in 11(18.33%). None of the patients with mild or no immunosuppression had any opportunistic infections (Table III).

Table II: CD4 cell count vs WHO clinical stage.

CD 4 cell count (n)	Stage 1	Stage 2	Stage 3	Stage 4
> 500 (7)	5	1	1	0
350 - 499 (7)	4	1	2	0
200 - 349 (28)	11	0	11	6
< 200 (60)	4	2	18	36
Total (102)	24	4	32	42

Table III: CD4 cell count and opportunistic infections.

CD4 Cell Count	Opportunistic Infections
> 500 (no immunosuppression)	0
350 - 499 (mild immunosuppression)	0
200 - 349 (advanced immunosuppression)	8
< 200(severe immunosuppresion)	71

Discussion

In this study on 102 patients with HIV, there were 60 patients (58.88%) with severe immunosuppression, 28 (27.45%) patients with advanced immunosuppression and 7 (6.86%) patients each with mild or no immunosuppression. Similar findings were noted by Bishnu *et al*[9] where 64% of the

patients were in the stage of severe immunosuppression; 21.67% were in advanced immunosuppression; 6.94% were in mild immunosuppression and 6.39% no significant immunosuppression respectively.

There were 74 (72.55%) patients in WHO clinical stage 3 and 4 indicating significant immunosuppression, 24 (23.5%) patients in WHO clinical stage 1 and 4 (3.92%) patients in clinical stage 2, which is comparable to the study conducted by Bishnu *et al*[9] where 59% of the patients were in clinical stage 3 and 4, 21.66% were in clinical stage 1 and 13. 05% were in clinical stage 2.

In this study, 54 (90%) patients with severe immunosuppression were in WHO clinical stages 3 and 4 whereas 5 (71.42%) out of the 7 patients with no significant immunosuppression were in WHO clinical stage 1. Bishnu *et al*[9] have showed that the mean CD4 count in clinical stage 4 was 106 cells/µl (severe immunosuppression) and that in clinical stage 1 was 338 cells/µl (advanced).

Amongst the asymptomatic patients, 7 (38.88%) of the 18 patients were in advanced immunosuppression. However, 77 (91.66%) out of the 84 symptomatic patients were in severe and advanced immunosuppression and 56 (66.66%) of these 84 patients were in severe immunosuppression. Kaslow *et al*, in their study found that symptoms such as fever and fatigue occurred with fall in CD4 cell counts and symptoms increased progressively and exponentially with further drop in CD4 counts[10].

In this study, it was observed that most of the opportunistic infections were present in patients with advanced and severe immunosuppression only. There were 71 Opportunistic Infections (OIs) observed amongst 60 patients with severe immunosuppression with GI infections being present in 28 patients (46.66%), followed by respiratory infections in 21 patients (35%) and CNS infections in 11 patients (18.33%). Amongst the 28 patients with advanced immunosuppression GI infections were the commonest (present in 8 patients). Singh *et al*[11], observed that oral candidiasis and significant weight loss were usually associated with low CD4 count.

Bishnu *et al*[9], noted that the mean CD4 count in sputum positive pulmonary tuberculosis cases was 84.83 cells/µl and sputum negative pulmonary tuberculosis was 107.89 cells/µl, whereas in TB meningitis it was 109.13 cells/µl. Mean CD4 count in patients with PJP was 94.45 cells/µl. In a study done in South Africa, the prevelance of OI was highest in patients with CD4 count of less than 50 cells/µl. Oral candidiasis and tuberculosis were common at CD4 cell count of more than 200 cells/microlitre and occasionally above 500 cells/microlitre[12].

However, Holmes *et al*[12] noted that tuberculosis can occur at any of CD4 cell count.

This study indicates the need for earlier recognition of HIV positive status and initiation of treatment before these patients go into significant immunosuppression or present with any opportunistic infections.

Summary and conclusions

Inspite of HIV infection being associated with significant morbidity and mortality in our country, there is paucity of Indian studies in this field. This study throws light on the advanced levels of immunosuppression at which patients present. Tireless efforts have to be made to detect HIV at an early stage. This will enable us to start HAART at an appropriate time. However monitoring of response to ART will specifically need focus on viral load testing.

References

1. Weinberg JL, Kovarik CL. The WHO Clinical Staging System for HIV/AIDS. *Virtual Mentor* 2010; 12 (3): 202.
2. UNAIDS. Global Report 2013 (Internet). 2013 (cited 2016 Feb 29); Available from: http://www.unaids.org/sites/default/files/en/media/unaids/contentassets/documents/epidemiology/2013/gr2013/UNAIDS_Global_Report_2013_en.pdf.
3. Bendavid E, Young SD, Katzenstein DA *et al*. Cost-effectiveness of HIV Monitoring Strategies in Resource-Limited Settings: A Southern African Analysis. *Arch Intern Med*. 2008; 168 (17): 1910.
4. Charles M, Boyle BA. Excess and access: the continuing controversy regarding HIV and health care in Africa. *AIDS Read*. 2002; 12 (7): 288-92.
5. NACO Annual report 2012-13 (Internet). (2013?) (cited 2016 Mar 14); Available from: http://www.naco.gov.in/upload/Publication/Annual%20Report/Annual%20report%202012-13_English.pdf.
6. PUNJABSACS. Overview of HIV-AIDS in Punjab (Till April 2015). (Internet). (2015?) (cited 2016 Mar 14); Available from: http://www.punjabsacs.org/docs/Overview%20of%20HIV-AIDS%20in%20Punjab%20%20(Till%20April%202015).doc.
7. Kumarasamy N, Vallabhaneni S, Flanigan TP *et al*. Clinical profile of HIV in India. *Indian J Med Res* 2005; 121 (4): 377-94.
8. WHO | Interim WHO clinical staging of HIV/AIDS and HIV/AIDS case definitions for surveillance (Internet). 2005 (cited 2016 Mar 14); Available from: http://www.who.int/hiv/pub/guidelines/casedefinitions/en/
9. Bishnu S, Bandyopadhyay D, Samui S *et al*. Assessment of clinico-immunological profile of newly diagnosed HIV patients presenting to a teaching hospital of eastern India. *Indian J Med Res* 2014; 139 (6): 903-12.
10. Kaslow RA. Infection with the Human Immunodeficiency Virus: Clinical Manifestations and Their Relationship to Immune Deficiency: A Report from the Multicenter AIDS Cohort Study. *Ann Intern Med* 1987; 107 (4): 474.
11. Singh A, Bairy I, Shivananda PG. Spectrum of opportunistic infections in AIDS cases. *Indian J Med Sci* 2003; 57 (1): 16-21.
12. Holmes CB, Wood R, Badri M *et al*. CD4 decline and incidence of opportunistic infections in Cape Town, South Africa: implications for prophylaxis and treatment. *J Acquir Immune Defic Syndr* 2006; 42 (4): 464-9.