

A retrospective study of clinical spectrum and treatment outcomes of HIV associated cancers in a tertiary care centre

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Abstract

Introduction: With the introduction and widespread availability of highly active anti-retroviral therapy (HAART), the landscape of HIV/AIDS has changed considerably. This is true for HIV-associated malignancies as well. Post-HAART, the incidence of Kaposi's sarcoma and central nervous system (CNS) lymphoma (among AIDS-defining cancers) decreased in parallel with AIDS-defining infections. On the other hand, the incidence of systemic non-Hodgkin's lymphoma (NHL) and cervical cancer decreased less than others and remains higher in HIV-infected patients than in the general population. Currently, malignancies are the most frequent underlying cause of death (around one-third) of HIV-infected patients. **Materials and Methods:** The study was a retrospective observational study which included all the patients with HIV and cancer attending the Oncology Department OPD, Govt Medical College, Jammu between January 2020 and December 2020. Data obtained from the case records was used to fill up the proforma which included the patient factors (Age, sex, performance status, BMI, substance abuse), HIV related parameters (Time since diagnosis of HIV, baseline CD4 counts, comorbid conditions, treatment with HAART), tumour related factors (Site, type of cancer, subtype, stage, prognostic factors depending on the histology) and treatment aspects (Type of treatment, any requirement of dose modifications, toxicity, response, compliance). **Results:** The study included 100 patients with HIV and cancer (43 female patients and 57 male patients) with an average age of 42 years. A majority of the patients (71%) were in the 31-40 years age group, as shown in Table 1. The mean BMI of the study group was 19.45 (Range: 10 -26.5). Thirteen of the forty-four patients (29.5 %) had poor general condition with a performance status of 3 or 4 by the ECOG (Eastern Cooperative Oncology Group) scale. All patients were already enrolled for anti-retroviral therapy. The mean time to presentation of cancer after the diagnosis of HIV infection was 5.4 years (Range: 2 months to 15 years). Thirty-two patients had Non-AIDS Defining Cancers (NADC) and twelve had AIDS defining cancers (ADC). **Conclusion:** In the HAART era, NADCs are more common than ADCs. Standard chemotherapy achieves a response rate of 50% in HIV-NHL cases and 46% in HIV patients with solid cancers. The study illustrates the need for prolonged surveillance for the development of cancer in HIV patients. Early initiation of HAART, optimal chemotherapeutic regimens, appropriate palliative care and nutritional support should form an integral part of the care of HIV patients with cancer.

Key Words: HAART, HIV, AIDS, NADC, ECOG.

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Introduction

With the introduction and widespread availability of highly active anti-retroviral therapy (HAART), the landscape of HIV/AIDS has changed considerably. This is true for HIV-associated malignancies as well. Post-HAART, the incidence of Kaposi's sarcoma and central nervous system (CNS) lymphoma (among AIDS-defining cancers) decreased in parallel with AIDS-defining infections[1]. On the other hand, the incidence of systemic non-Hodgkin's lymphoma (NHL) and cervical cancer decreased less than others and remains higher in HIV-infected patients than in the general population. Currently, malignancies are the most frequent underlying cause of death (around one-third) of HIV-infected patients[2].

The situation in a developing country like India is suboptimal. Lack of widespread availability of diagnostic facilities, access to HAART, and cancer therapy were major limitations[3]. Currently, India has the 2nd highest number of people with HIV/AIDS (PWHAs).

National AIDS Control Organization (NACO), the nodal agency to control the spread of HIV/AIDS in India, estimates the current prevalence of HIV infection to be 0.27%[4]. The assessment of problem load of HIV-associated malignancies in India is limited by lack of quality epidemiologic data collected in this regard[5].

We wanted to assess the pattern of cancers, clinical profile and the treatment outcomes in the cancer patients with HIV.

Materials and methods

The study was a retrospective observational study which included all the patients with HIV and cancer attending the Oncology Department OPD, Govt Medical College, Jammu between January 2020 and December 2020. Data obtained from the case records was used to fill up the proforma which included the patient factors (Age, sex, performance status, BMI, substance abuse), HIV related parameters (Time since diagnosis of HIV, baseline CD4 counts, comorbid conditions, treatment with HAART), tumour related factors (Site, type of cancer, subtype, stage, prognostic factors depending on the histology) and treatment aspects (Type of treatment, any requirement of dose modifications, toxicity, response, compliance).

An informed consent was obtained from all patients. Cancers were diagnosed and classified based on histopathology reports. The AIDS defining cancers were invasive cervical cancers, Non-Hodgkin's lymphoma (Including primary CNS lymphoma, primary effusion lymphomas) and Kaposi's sarcoma. Other cancers are considered to

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be Non-AIDS defining cancers. For incomplete case records, the pending data was collected from concerned labs and patient's relatives were contacted for other relevant information.

Statistical Analysis

Statistical analysis was done using IBM SPSS software (v-21). Categorical values were summarized in terms of frequencies and proportions. Descriptive analysis was done for continuous variables

using mean and standard deviations. Kaplan Meier curves were used for comparison of survival between patient subgroups.

Results

The study included 100 patients with HIV and cancer (43 female patients and 57 male patients) with an average age of 42 years. A majority of the patients (39%) were in the 31-40 years age group, as shown in Table 1.

Table 1: Age wise distribution

S.No	Age Group	Number of patients	Percentage
1	0-10 years	0	0
2	11-20 years	0	0
3	21-30 years	4	4
4	31-40 years	39	39
5	41-50 years	33	33
6	51-60 years	18	18
7	61-70 years	6	6

Table 2: Distribution of the Cancer Types in Patients with HIV and Cancer

S.No	Type of cancer	Number of patients	Percentage
1	Non Hodgkins lymphoma	30	30%
2	Head and Neck cancer	12	12%
3	Colorectal Cancer	7	7%
4	Carcinoma Cervix	9	9%
5	Carcinoma Penis	9	9%
6	Appendicular Mucinous	4	4%
7	Carcinoma Breast	4	4%
8	Carcinoma Anal Canal	4	4%
9	Multiple Myeloma	4	4%
10	Soft Tissue Sarcoma	3	3%
11	Carcinoma Gall Bladder	3	3%
12	Carcinoma Esophagus	3	3%
13	Carcinoma Ovary	2	2%
14	Carcinoma stomach	2	2%
15	GIST	2	2%
16	Hodgkins Lymphoma	2	2%

Table 3: NHL Subtypes in HIV Patients

S.No	NHL Subtypes	N (%)
1	DLBCL	12 (40%)
2	Extra nodal MZL	6 (22%)
3	Primary CNS Lymphoma	2 (7%)
4	Plasmablastic Lymphoma	2 (7%)
5	Burkitt Like	4 (14%)
6	Subtype-Not Known	4 (14%)

Table 4: Stage Wise Distribution of Lymphomas in HIV Patients

S.No	Lugano stage of Lymphoma	N (%)
1	1	12 (44%)
2	2	4 (14%)
3	3	4 (14%)
4	4	8 (28%)

Table 5: Stage Wise Distribution of Solid Cancers in HIV Patients

S.No	TNM stage of Solid Tumor	N (%)
1	1	0 (0%)
2	2	8 (13%)
3	3	11 (37%)
4	4	30 (50%)

The mean BMI of the study group was 19.45 (Range: 10 -26.5). Thirteen of the hundred patients (29.5 %) had poor general condition with a performance status of 3 or 4 by the ECOG (Eastern Cooperative Oncology Group) scale. All patients were already

enrolled for anti-retroviral therapy. The mean time to presentation of cancer after the diagnosis of HIV infection was 5.4 years (Range: 2 months to 15 years). Thirty-two patients had Non-AIDS Defining Cancers (NADC) and twelve had AIDS defining cancers (ADC).

The most common malignancy seen was Non-Hodgkin's lymphoma, accounting for thirty cases. None of the patients had Kaposi's sarcoma. Head & neck cancers, carcinoma penis, anal cancer, cervical

cancer and colorectal cancers were the common solid tumours as shown in table 2. Meier Plot Comparing the Survival Curves of HIV-Solid Cancer Patients on Chemotherapy versus Patients on Supportive Care among the Non-Hodgkin's lymphoma patients, the pathological subtype was available for twelve of them. DLBCL lymphoma was the most common subtype (10 cases). The other subtypes included Burkitt like lymphoma, primary CNS lymphoma, Plasmablastic Lymphoma and extranodal marginal zone lymphoma.

In the HIV patients with Non-Hodgkin's lymphoma, extranodal presentations were more common than nodal presentations. Of the 28 cases of NHL only three had nodal presentation whereas eleven had extranodal presentation. B symptoms (Fever, loss of weight, night sweats) were present in eight of the fourteen cases. The stage wise distribution of the lymphomas and solid tumours is shown in table 4 and 5. Majority of the Non-Hodgkin's lymphoma patients presented with stage 1 disease, while most of the solid tumours were stage 4 on presentation. All patients were already enrolled for Anti-Retro Viral Therapy (ART), with an average CD4 count of 363.

Among the 28 NHL patients, 14 received chemotherapy and had a median survival of 6 months (95% CI: 5.2 to 6.7 months), while the other 14 received only supportive care on account of their poor general condition and had median survival of 1.5 months (95% CI: 0.2 to 2.7 months). The chemotherapy regimens included CHOP, CVP, R-CHOP and R-CHOP-E. 4 patients completed treatment schedule with 2 achieving partial response. The survival comparison between the patients on chemotherapy and best supportive care is shown in the following Kaplan Meier plot (Table 5).

Discussion

Malignancies in HIV patients are a major challenge to health care providers. There are various guidelines available for the management of cancers in PLWHA, foremost among them being BHIVA (British HIV Association) guidelines. These guidelines recommend that PLWHA patients with cancer should be treated at a high-volume centre by a multi-disciplinary team that includes haematologists, oncologists, surgical oncologists, radiation oncologists and HIV physicians [6]. The management includes prompt initiation of antiviral agents, anti-microbial agents against *Pneumocystis carinii*, *Mycobacterium avium-intracellulare* (Depending on the CD4 counts) and chemotherapy. HAART enables the use of full dose standard chemotherapy, including high dose chemotherapy and hematopoietic stem cell transplants. HIV infected patients with cancer receiving chemotherapy would also require azole antifungals, anti-herpes prophylaxis (In patients with past herpetic infections) and appropriate vaccinations [7]. In this study, we have documented the clinical spectrum of cancers occurring in PLWHA in South India. In the Pre HAART era, the majority of cancers in PLWHA were ADCs (Like aggressive NHL, invasive cervical cancers, Kaposi sarcoma and primary CNS lymphomas) due to their low CD4 counts and profound immunosuppression. But in the HAART era, NADCs occur more commonly than ADCs, since PLWHA live longer and hence tend to develop age related and substance abuse related cancers like the general population [8]. The incidence of ADCs has declined by 70% after the introduction of HAART. In this study, thirty two patients (72.7%) had Non AIDS Defining Cancers (NADC) and twelve had AIDS defining cancers (ADC). This is higher than that reported by Dhir et al in a study involving patients with HIV and cancer in western India where NADCs accounted for 43% [9].

The most common malignancy in this study was Non-Hodgkin's Lymphoma (B-cell lineage), similar to other studies by Dal Maso et al and Dhir et al. Extranodal presentations were more common than nodal presentations. B symptoms were present in 57% of the NHL cases. DLBCL lymphoma was the most common NHL subtype, comprising 36% of the NHL cases. This is in accordance to the findings in the study by Shiels et al where DLBCL (Diffuse large B cell lymphoma) was found to be the most common NHL in HIV

patients. Carcinoma penis, cervical cancers and oropharyngeal cancers which are considered to be HPV (human papilloma virus) related constituted 20.4% of the cases, suggesting a preventive role for HPV vaccination in these cases.

The mean time to presentation of cancer after the diagnosis of HIV was 5.4 years and hence PLWHA have to be under prolonged surveillance for cancer. The mean BMI was 19.45 and about 52.2% had a BMI <20 with recent weight loss >5% of their body weight, thus placing them in the cachectic category. This highlights the need to address the nutritional deficiencies in these patients who often have significant malnutrition due to the HIV, cancer, infections and poor social support. Nearly 29.5% had a poor performance status (ECOG scale 3/4), thus precluding upfront chemotherapy. All patients were already enrolled on anti-retroviral therapy. Early initiation of ART results in better quality of life and better performance status, thus enabling use of more intensive chemotherapy regimens. None of the patients in this study had significant drug interactions involving ART and chemotherapy [10].

Conclusion

In the HAART era, NADCs are more common than ADCs. The most common malignancy in HIV patients is NHL, with plasmablastic subtype being the commonest in this study. Extranodal presentations are more common than nodal presentation. Standard chemotherapy achieves a response rate of 50% in HIV-NHL cases and 46% in HIV patients with solid cancers. The study illustrates the need for prolonged surveillance for the development of cancer in HIV patients. Early initiation of HAART, optimal chemotherapeutic regimens, appropriate palliative care and nutritional support should form an integral part of the care of HIV patients with cancer.

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