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Research Article

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.
Materials and methods: The study was a retrospective observational study which included all the patients with HIV and cancer attending the Oncology Department OPD Department of Radiation Oncology, Government Madurai Medical College, Madurai between January 2024 and December 2024. 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 200 patients with HIV and cancer (86 female patients and 114 male patients) with an average age of 42 years. A majority of the patients (39%) were in the 31-40 years age group. The mean BMI of the study group was 19.45 (Range: 10 -26.5). 59 of the 200 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). 122 patients had Non-AIDS Defining Cancers (NADC) and 78 had AIDS defining cancers (ADC).
Conclusion: In the HAART era, NADCs are more common than ADCs. The most common malignancy in HIV patients is NHL, with DLBCL (Diffuse Large B-Cell Lymphoma) subtype being the commonest in this study. Extranodal presentations are more common than nodal presentation. Standard chemotherapyachieves 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, radiotherapy protocols, appropriate palliative care and nutritional support should form an integral part of the care of HIV patients with cancer.

Keywords: Highly Active Anti-Retroviral Therapy, HIV-Associated Malignancies, Non-Hodgkin's Lymphoma.

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 cancertherapy were major limitations.Currently, India has the 2nd highest number of people with HIV/AIDS.[3]

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%. The assessment of problem load of HIV-associated malignancies in India is limited by lack of quality epidemiologic data collected in this regard.[4,5]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 Department of Radiation Oncology, Government Madurai Medical College, Madurai between January 2024 and December 2024.

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 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 200 patients with HIV and cancer (86 female patients and 114 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	8	4
4	31-40 years	78	39
5	41-50 years	66	33
6	51-60 years	36	18
7	61-70 years	12	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	60	30%
2	Head and Neck cancer	24	12%
3	Colorectal Cancer	14	7%
4	Carcinoma Cervix	18	9%
5	Carcinoma Penis	18	9%

6	Appendicular Mucinous	8	4%
7	Carcinoma Breast	8	4%
8	Carcinoma Anal Canal	8	4%
9	Multiple Myeloma	8	4%
10	Soft Tissue Sarcoma	6	3%
11	Carcinoma Gall Bladder	6	3%
12	Carcinoma Esophagus	6	3%
13	Carcinoma Ovary	4	2%
14	Carcinoma stomach	4	2%
15	GIST	4	2%
16	Hodgkins Lymphoma	4	2%

Table 3: NHL Subtypes in HIV Patients

S.No	NHL Subtypes	N (%)
1	DLBCL	24 (40%)
2	Extra nodal MZL	12 (20%)
3	Primary CNS Lymphoma	4 (6.66%)
4	Plasmablastic Lymphoma	4 (6.66%)
5	Burkitt Like	8 (13.33%)
6	Subtype-Not Known	8 (13.33%)

Table 4: Stage Wise Distribution of Lymphomas In HIV Patients

S.No	Lugano stage of Lymphoma	N (%)
1	1	8 (13.3%)
2	2	24 (40%)
3	3	12 (20%)
4	4	16 (26.6%)

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	16 (13%)
3	3	45 (37%)
4	4	61 (50%)

The mean BMI of the study group was 19.45 (Range: 10 -26.5). 59 of the 200 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). 122 patients had Non-AIDS Defining Cancers (NADC) and 78had AIDS defining cancers (ADC) as shown in Table 2.

Among the 60 NHL patients,56 received chemotherapy and had a median survival of 30 months (95% CI: 24 to 48 months), while the other 4 received only supportive care on account of their poor general condition and low CD4 count, had median survival of 6 months (95% CI: 1 to 9 months).The chemotherapy regimens included CHOP, CVP, R-CHOP and R-CHOP-E. After completion of chemotherapy depending upon the response assessment using Deuville's Score, patient were treated with either ISRT (Involved Site Radiotherapy) or INRT (Involved Node Radiotherapy) to dose of 36 to 40 Gy. All 56 patients completed the planned treatment schedule, while 4 patients had persistent or residualdisease.

The cervical cancer patients were treated as per the recommended protocol. Brachytherapy is avoided to them as per the institutional protocol. They were given SBRT (Stereotactic Body Radiotherapy) Boost after external beam radiotherapy (EBRT) as substitute to brachytherapy. All other solid tumors were treated as per the recommended treatment protocol. There is no variation in the dosage of radiotherapy in treating HIV patients with solid tumors, but chemo dosages were altered

depending on patient's general condition and CD4 counts. The survival depends upon the initial stage, treatment completion, response rate and general condition of the patient. The Stage wise comparison of solid tumors in HIV patients is shown in 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 haemato-oncologists, surgical oncologists, radiation oncologists and HIV physicians.[6] The management includes prompt initiation of antiviral agents, anti-microbial agents against Pneumocystis carinii, mycobacterium aviumintracellulare (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.[7]

HIV infected patients with cancer receiving chemotherapy would also require azole antifungals, anti-herpes prophylaxis (In patients with past herpetic infections) and appropriate vaccinations. 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, one hundred and twenty two patients (61%) had Non AIDS Defining Cancers (NADC) and seventy eight (39%) had AIDS defining cancers (ADC),as shown in Table 2. This is higher than that reported by Dhir et al ina study involving patients with HIV and cancer in western India where NADCs accounted for 43%.The most common malignancy in this study was Non-Hodgkin`s Lymphoma (B-cell lineage) 30%, 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 40% of the NHL cases, as shown in Table 3. Nearly 47% of NHL cases are in stage 3 and 4, as shown in Table 4. This is in accordanceto 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, anal canal cancers, cervical cancers and oropharyngeal cancers which are considered to be HPV (human papilloma virus) relatedconstituted 34% of the cases, suggesting a preventive role for HPV vaccination in these cases.[9]

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 patientsin 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 DLBCL (Diffuse Large B-Cell Lymphoma) subtype being the commonest in this study. Extranodal presentations are more common than nodal presentation. Almost 50% of the solid tumors in HIV patients presented in stage 4 disease, as shown in Table 5. Standard chemotherapyachieves 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, radiotherapy protocols, appropriate palliative care and

nutritional support should form an integral part of the care of HIV patients with cancer.

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