Analysis of Malignancies in HIV Positive Patients: Observational Study in a Tertiary Care Hospital of Jharkhand

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ABSTRACT

BACKGROUND
There is scarcity of data on the frequency of malignancies in HIV infected individuals from Jharkhand. We wanted to analyse the pattern of malignancies in patients with HIV-AIDS based on their age and sex and document the CD4 counts at the time of diagnosis of the malignancy.

METHODS
We conducted a retrospective analysis of data of all patients presenting with a malignancy and coexisting HIV-AIDS from January 2017 through December 2019 were analysed initially. The pathological diagnosis, clinical stage, and the CD4 cell count at diagnosis, were noted.

RESULTS
There was a total of 150 patients. Of that total, 80 (53%) were men, and 70 (47%) were women. The mean age was 45 years (range 20 - 65 years). The three most common malignancies observed were Non-Hodgkin's lymphoma (24%), squamous cell carcinoma (SCC) of cervix (22%) and squamous cell carcinoma of head and neck (19%). At lower CD4 counts (<250 cells/µL), NHL was the most frequent malignancy. At well preserved CD4 (>250 cells/ µL), HNSCC and SCC of cervix were more frequently observed.

CONCLUSIONS
In present study, AIDS defining malignancies were more common than non-AIDS defining malignancies. A comprehensive approach towards the treatment of these patients giving adequate therapy for both the conditions, is the need of the hour.

KEYWORDS
AIDS Defining Malignancies, HAART, HIV, Non-AIDS Defining Malignancy, Non-Hodgkin's Lymphoma

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BACKGROUND

Malignancies are more common in immunocompromised individuals as compared to the general population. In developed countries, 34% of AIDS patients suffer from aggressive malignancies which are resistant to treatment and are often fatal.[1] On the other hand, in India, the incidence of malignancies in patients with HIV is only 3%–4% which is attributed to under- diagnosis and early deaths from opportunistic infections.[1] The overall risk of all malignancies is increased by two-to-three fold in people with HIV infection and the relative risk as compared to normal population is more (60 – 200 times) for AIDS-defining malignancies such as non-Hodgkin lymphoma (NHL).[2,3] HIV prevalence in India is estimated at 0.22% (0.16% – 0.30%) and of Jharkhand is 0.14% in 2017.[4] HIV-associated cancers are broadly divided into two type's acquired immune deficiency syndrome (AIDS) - defining cancers (ADC) and non-AIDS-defining cancers (NADC). ADC include non-Hodgkin's lymphoma (NHL), invasive cervical carcinoma, and Kaposi's sarcoma (KS). NADC include lung cancer, anal cancer, Hodgkin's lymphoma, etc. NHL remains the most common cancer in patients with HIV worldwide. Risk factors for cancer in HIV include immunosuppression, oncogenic potential of HIV, co-infection with other oncogenic virus such as hepatitis B and C, human herpes virus-8 (HHV-8) infection, human papilloma virus (HPV), Epstein-Barr virus (EBV) etc.

There has been a significant decrease in the number of HIV-AIDS–related deaths in recent years because of the remarkable increase in the use of antiretroviral therapy (ART).[4] However, newer challenges have emerged with improved survival, such as an increasing number of patients being diagnosed with malignancies. In the current highly active antiretroviral therapy (HAART) era, the pattern of malignancies in people living with HIV-AIDS has changed compared with the pre-HAART era.[5] In the developed countries, incidence of AIDS-related malignancies among patients who received HAART therapy is decreasing,[5,6] and.[7] However, the spectrum and clinical correlates of malignancies among HIV-infected Indian patients remain to be fully characterized.[8,9] According to Indian data, NHL is the most common cancer overall and Kaposi's sarcoma is rare. Increasing access to ART is expected to decrease the overall incidence of cancer in this population, but the spectrum of cancer in people living with HIV in India needs to be better understood for effective screening. In this study, we present the observations made in the patterns of malignancies seen in HIV positive patients at a tertiary care hospital in state of Jharkhand. The aim of the study was to analyse the pattern of malignancies in patients with HIV-AIDS based on their age and sex and to document the CD4 counts at the time of diagnosis of malignancy. The spectrum of malignancies in this group of patients differs from that in the general population. In addition, the pattern and the magnitude of malignancies differ in different parts of the world.[10] In this study, we have analysed the pattern of malignancies in patients with HIV-AIDS in a regional cancer Centre in India.

METHODS

We retrieved data from our institution's medical records department on all patients who had HIV-AIDS and had been diagnosed with a malignancy. Data of all patients presenting with a malignancy and coexisting HIV-AIDS from January 2017 through December 2019 were analysed initially. We analysed the case records of 150 HIV positive patients registered at our hospital. The pathological diagnosis, clinical stage and the CD4 cell count at diagnosis were noted. We analysed the correlation between the patients' CD4 counts and malignancies sub classified as AIDS-defining cancers (ADCs; aggressive B-cell non-Hodgkin lymphoma (NHL) and cervical cancer) or non–AIDS defining cancers (NADCs; all other malignancies other than aggressive NHL and carcinoma cervix were defined as NADC). A statistical analysis was performed using SPSS Statistics for Windows, version 23 (IBM Corp, Armonk, NY). The study was carried out in accordance with the Declaration of Helsinki and Good Clinical Practice Guidelines.

RESULTS

There was a total of 150 patients. Out of these 80 (53%) were men, and 70 (47%) were women. The mean age was 45 years (Range 20-65 years). Overall, the three most common malignancies observed were Non-Hodgkin's lymphoma, squamous cell carcinoma (SCC) of cervix and squamous cell carcinoma of head and neck.

Most common malignancy was Non-Hodgkin's lymphoma (24%) (36 out of 150 patients). 14 patients (40%) were of nodal disease, 18 patients (50%) were of extra nodal disease and 4 patients (10%) had primary CNS lymphoma (PCNSL). Relatively higher frequency of extra nodal disease was seen in the study group. Diffuse large B cell lymphoma (DLBCL) comprised the most frequent type of lymphoma (22 patients, 60%) followed by Burkitt's lymphoma (4 patients,) and Plasmablastic lymphoma (2 patients). Most of the DLBCL were germinal center (GC) type (17 out of 22, 78%). All patients, except one, had B symptoms at the time of presentation.

Malignancy	Incidence
Non-Hodgkin's lymphoma	32%
Squamous Cell carcinoma of head and neck (HNSCC)	30%
SCC of anal canal	9%
Adenocarcinoma of lung	8%
Carcinoma of Penis	5%
Carcinoma of urinary bladder	5%
Acute leukemia	3%
Hepatocellular carcinoma	3%
Seminoma testis	2%
Adenocarcinoma of Prostate	2%
SCC Skin	1%

Table 1. Observations among Male Patients

33 patients (22%) were of SCC of cervix. Majority of the patients presented with stage II or stage III disease. 27 patients (19%) were found to be of HNSCC (Head and Neck Squamous Cell Carcinoma). Almost all the patients gave history of consumption of tobacco related products. Majority

of patients had carcinoma of buccal mucosa (14 patients, 52%) and tongue (9 patients, 33%) and only 2 patients each of tonsil and pyriform fossa were observed. These observations indicate that HNSCC seen in the study group are tobacco related and not associated with Human Papilloma virus (HPV) related which mostly involves the laryngopharyngeal region.

The high frequency of HNSCC is due to the high prevalence in the general population and coexistence of risk factors (tobacco chewing and smoking). SCC of anal canal is seen at higher frequency in HIV patients as it is related to HPV infection.

Malignancy	Incidence
SCC Cervix	47%
NHL	14%
Invasive ductal carcinoma of breast	11%
Acute leukemia	7%
SCC vulva	5%
HNSCC	4%
Adenocarcinoma endometrium	3.5%
Adenocarcinoma ovary	3%
HCC	2.5%
Soft tissue sarcoma	2%
Hodgkin lymphoma	1%

Table 2. Observations among Female Patients

Other gynaecological malignancies (carcinoma ovary and endometrium) were infrequently observed. Carcinoma breast in 6 patients (9.5%). HCC was seen in 2 patients (3%) who were co-infected with hepatitis B.

CD4 Counts	Total No. of Patients (n)	Most Common Malignancies
<=100	20	NHL (70%)
101-250	30	NHL (50%)
251-500	60	SCC cervix (40%), HNSCC (30%)
>500	40	SCC cervix (24%), HNSCC (20%)

Table 3. Correlation with CD4 T Cell Count

At lower CD4 counts (<250 cells/µL), NHL was the most frequent malignancy. At well preserved CD4, HNSCC and SCC of cervix were more frequently observed. The median CD4 count was 150 cells/µL in Non-Hodgkin's Lymphoma patients. All the 3 patients with PCNSL had a CD4 T cell count < 100 cells/µL. The median CD4 count was 425 cells/µL in HNSCC patients. The median CD4 T cell count was 280 cells/µL in squamous cell carcinoma of cervix patients.

DISCUSSION

The present study analyses the patterns of AIDS Defining Cancers (ADC) and NADC malignancies seen in HIV positive patients at a tertiary care hospital in state of Jharkhand. AIDS defining cancers were seen more frequently than non-AIDS defining cancers. The two most common malignancies observed during the course of study were NHL and SCC of cervix. The third ADC, Kaposi's sarcoma, however, was not observed.

The study proved that Kaposi sarcoma is quite rare in the Indian population, and there was no case of Kaposi sarcoma diagnosed in the samples taken. Several researches done in the past have similar findings across India. Dhir et al which is one of the remarkable published series in India also reported that no case of Kaposi sarcoma was reported when they evaluated around 251 patients with HIV-AIDS and malignancy.[8] Dhir added that findings had its roots with low seroprevalence of Kaposi sarcoma-associated herpesvirus in the Asian population.[8] The same story were explained in three studies done in southern India in which they did not report the incidence of Kaposi Sarcoma in their series of HIV-AIDS patients with malignancies.[11-13] Such argument were further strengthened by Sachdeva et al when they found similar results in north India.[14] The incidence of other immunodeficiency-related malignancies was identical to those reported in other studies in the literature.[8,16]

Western literature have recognised the increasing incidence of NADC but it also important that ADCs with a total of 48% of all malignancies, remained the most common malignancies found amongst HIV-AIDS population.[15-17] Indian study also supports the argument.[8,17] With the widespread availability of generic HAART, the incidence of ADCs may decrease in future. Other non-AIDS defining malignancies were also observed with increased frequencies (HNSCC, SCC of anal canal, IDC of breast and Adeno Carcinoma of lung). The increasing incidence of the NADC is partly attributed to the increasing incidence of these malignancies in the general population. Powles et al in his study showed that in HAART era there is substantial decline in the ADC as compared to NADC.[18] Another major study have been conducted during 2001 to 2005 is of Dhir et al who while studying pattern of cancer at their HIV cancer clinic recorded site-specific Population Incidence Ratio (PIR). It was observed that NHL had the highest PIR followed by anal canal cancer and HL.[8] The unusually high occurrence of HNSCC in present study reflects its very high prevalence in the general population and concurrent presence of risk factors (tobacco, chewing and smoking). Smoking, use of alcohol and oncogenic virus co-infection, such as human papilloma virus (HPV) or hepatitis B and C viruses are traditional risk factors for cancer.[19-22]

Agarwal et al studied pattern of lymphoma in 35 HIV positive patients at Tata Memorial Hospital, Mumbai and found 24 patients with NHL, seven Hodgkin's lymphoma and four plasmacytomas.[9] We identified 22 cases with DLBCL, 4 case of CNS lymphoma, 4 Burkitt's lymphoma and 2 plasmablastic lymphoma. In the current study Non-Hodgkin's lymphoma and HNSCC were most common in male and carcinoma cervix and NHL was most common in female. It differs from the distribution among non-infected Indian patients where cancers of lip and oral cavity and lungs are common in male and cancers of the cervix and breast are common in female.

The study also highlights that Mean CD4 + cell count was significantly lower in patients with AIDS Defining Cancer (ADC) as compared to Non-AIDS Defining Cancer (NADC). At relatively lower CD4 counts, NHL was frequently observed while at well preserved CD4 counts, SCC of cervix and HNSCC were more common. Biggar et al reported that there

is inverse relationship between risk of cancer and CD4+ count for all AIDS defining cancers except cervical cancer,

Where there was no relationship noted between CD4+ and cancer Incidence.[10] Only in few cancers such as in Kaposi's sarcoma and some type of NHL there was already explained mechanism by which a low CD4+ count is associated with risk of cancers, in others mechanisms are not clear.[23] In the present study, patients had advanced stage disease at the time of diagnosis and had lower CD4 cell count. This finding is concordant with the high frequency of AIDS-related malignancies, which are more frequent in patients with advanced immunodeficiency defined by a low CD4 cell count.[24]

CONCLUSIONS

HIV related malignancies remain an under-reported public health problem. In the present study, AIDS defining malignancies were more common than non-AIDS defining malignancies. Non-Hodgkin's lymphoma was the most common malignancy in both male and female HIV positive patients. It is possible that with the continued roll-out of highly active antiretroviral therapy, the incidence of HIV-associated malignancies will decrease. A comprehensive approach towards the treatment of these patients giving adequate therapy for both the conditions, is the need of the hour.

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