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RESEARCH ARTICLE

Prevalence of HIV in Patients with Malignancy and of Malignancy in HIV Patients in a Tertiary Care Center from North India

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Abstract: ***Background and Objectives*:** People living with HIV/AIDS are at an increased risk of developing cancer. The goals of this study were to obtain data on the prevalence of HIV in the cancer population and *vice versa* at a major tertiary cancer and HIV center in North India.

***Methods*:** This cross-sectional study was conducted over a 3-year period from July 2013 to June 2016, wherein successive HIV positive patients from an anti-retroviral therapy (ART) center were screened for malignancy. Simultaneously, successive cancer patients at the cancer center were screened for HIV. Baseline demographic details, risk factors, and laboratory investigations were obtained for all the patients.

***Results*:** Among the 999 HIV-positive patients at the ART center, the prevalence of malignancy was 2% (n=20; 95% confidence interval (CI) 1.13, 2.87). Among the 998 patients with a malignancy, the prevalence of HIV infection was 0.9% (n=9; 95% CI 0.31, 1.49). Weight loss, loss of appetite, and fever were the most common symptoms in patients with HIV and cancer. Among 29 patients with HIV and cancer, AIDS-defining cancer was found in 19 patients; non-Hodgkin's lymphoma was the most common malignancy reported (n=13).

***Interpretation and Conclusion*:** There is a low prevalence of HIV in cancer patients as well as a low prevalence of cancer in HIV patients. AIDS-defining cancers remain much more common than non-AIDS-defining cancers. With the increased coverage of ART, it is expected that non-AIDS-defining cancers will increase, as is evident from data from more developed countries.

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1. BACKGROUND

Human immunodeficiency virus (HIV) infection is a risk factor for cancer [1, 2]. HIV-associated cancers can be divided into acquired immune deficiency syndrome (AIDS)-defining cancers (ADC) and non-AIDS-defining cancers (NADC) [2]. The availability of effective antiretroviral therapy (ART) has lowered the incidence of cancer but there has been a simultaneous increase in the life expectancy of people living with HIV [3]. Consequently, the overall incidence of cancer and AIDS-defining cancer has stabilized over the last two decades (except invasive cervical cancer), while there has been an absolute increase in NADC [2-6]. HIV-associated cancer is one of the leading causes of death in HIV patients [7-9].

ADC include non-Hodgkin's lymphoma (NHL), invasive cervical carcinoma, and Kaposi's sarcoma (KS) [10]. NADC include lung cancer, anal cancer, Hodgkin's lymphoma, *etc.* The standardized incidence ratio (which compares the cancer rate in patients with HIV to the expected rate in the general population) [11] varies from 2 in lung cancer to 498 in Kaposi's sarcoma. NHL remains the most common cancer in patients with HIV worldwide [2, 12].

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Risk factors for cancer in HIV include immunosuppression, oncogenic potential of HIV [13], co-infection with other oncogenic virus such as hepatitis B and C [13], human herpes virus-8 (HHV-8) infection [14, 15], human papilloma virus (HPV) [16], Epstein-Barr virus (EBV) [17, 18], *etc*. HIV can also sensitize the cells to the oncogenic potential of tobacco, as suggested by an increase in the risk of lung cancer in people living with HIV (three times the general population) after adjustment for smoking status [13].

In 2016, there were 36.7 million people living with HIV worldwide; 2.1 million of these lived in India [19, 20]. Based on regional records, NHL is the most common cancer overall [21-24] and Kaposi's sarcoma is rare [23]. Increasing access to ART [25] 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.

We aim to look at the prevalence and spectrum of cancer in HIV patients at a tertiary care referral center in North India.

2. METHODS

From July 2013 to June 2016, we used a structured history and physical examination to screen successive adult (≥18 years) HIV-positive patients, irrespective of whether or not on any anti-retroviral therapy (ART), who presented at the ART center at the hospital for malignancy. The institute's ethics committee approved the protocol. Written informed consent was obtained from all the participants prior to their participation in the study.

Baseline demographic data were recorded regarding education, occupation, marital status, status of spouse and children, and likely mode of transmission. CD4 count was assessed for all the patients with HIV and cancer at the ART center. CD4 cell counts were measured by flow cytometry using BD FACS CALIBUR and fluorescein monoclonal antibodies (Becton Dickenson Biosciences, San Jose, CA, USA).

We assessed for known risk factors for malignancies such as current or former smoking, tobacco chewing, and alcohol intake. Those suspicious for malignancy were further evaluated with radiological investigations such as X-ray, ultrasound, computed tomography (CT) scan, magnetic resonance imaging (MRI), and positron-emission tomography (PET)-CT scan of the region of interest. All the malignancies were confirmed by histopathological examination. The time since the diagnosis of HIV and malignancy was recorded for all the patients. The overall prevalence of malignancy in HIV was calculated.

All the consecutive patients who presented at the cancer center with a confirmed diagnosis of a malignancy were screened for HIV antibodies using ELISA. All patients, irrespective of type and stage of malignancy were included in the study after due consent. Biopsy reports of all the patients diagnosed elsewhere were reviewed at this hospital for confirmation of diagnosis. The patients who tested positive for HIV were referred to the ART clinic at the All India Institutes of Medical Sciences (AIIMS) for HIV treatment and follow-up.

The study was continued till 1000 patients each were recruited at the ART center and the cancer center respectively.

All the patients with HIV and cancer were followed-up for treatment response and outcome for one year post-enrollment.

The data were recorded in a predesigned Excel spreadsheet. All the participants were given a unique code number. We calculated the prevalence of cancer in the HIV patients and the prevalence of HIV infection in patients with cancer over the three-year period. The descriptive statistics were calculated, including means and standard deviations for the continuous variables and percentages for the categorical variables. One-way ANOVA with Bonferroni's correction was used to find significant differences in the data following parametric distribution, while the Wilcoxon rank-sum test was used to find differences in CD4 counts between the groups.

3. RESULTS

There were 999 HIV-positive patients enrolled from the ART clinic and 998 patients from the cancer clinic. Most of the patients at the ART center were males, whereas most patients at the cancer center were females.

Of the 999 HIV-positive patients, 20 patients were diagnosed with a malignancy.

The overall prevalence of cancer in the HIV patients was 2% (20/999) [95% confidence interval (CI)I 1.13, 2.87].

Of the 998 cancer patients, 9 patients had HIV infection. The overall prevalence of HIV in the cancer patients was 0.9% (9/998) (95% CI 0.31, 1.49). For the analysis, we divided the patient population into three groups: HIV only (group 1, n=979), cancer only (group 2, n=989), and HIV and cancer (group 3, n=29) (Table **1**).

Most of the patients in the three groups did not smoke or consume significant amounts of alcohol. The patients with HIV and cancer were older than those with HIV only (44.8±10.5 *vs* 36.7±9.2 years, p-value <0.05).

Almost half of the patients with HIV and cancer had fever, involuntary weight loss, and loss of appetite in the preceding six months, while only one-third of the patients in the HIV only group had these symptoms. There was no significant difference in the CD4 counts in groups 1 and 3 at the time of diagnosis of cancer (median CD4 count 246 vs 188, p-value >0.05).

Among the patients with HIV and cancer (n=29), 22 were male and 7 were female. Overall, 19 patients had AIDS-defining cancers while 10 had non-AIDS-defining cancers. The most common malignancy was non-Hodgkin's lymphoma (13/29) followed by invasive cervical carcinoma (6/29). No case of KS was observed.

There was only one case of hepatitis B co-infection in patients with HIV and cancer. At one-year follow up, 19 patients were alive, 8 patients had died, and 2 patients could not be traced.

Table 1. Demographic variables, risk factors and malignancy distribution.

Variables	HIV Only n=979	Cancer Only n=989	HIV and Cancer n=29
Age (years)	36.7±9.2	48.5±13.7	44.8±10.5
Male (%)	740 (75.5%)	361 (36.5%)	22 (75.8%)
CD4 (cells/mm^3)	246 (155,377)		188 (101,411)
Marital status			
• Married	361 (37%)	909 (92%)	25 (93%)
• Unmarried	618 (63%)	80 (8%)	4 (7%)
Transmission route			
• Heterosexual	902 (92%)	-	21 (72.4%)
• Mother to child transmission	15 (1.5%)		-
• Other	62 (6.3%)		8 (27.6%)
Smoking			
• Current smoker	47 (5%)	6 (0.6%)	3 (10.3%)
• Past smoker	187 (19%)	43 (4.3%)	8 (27.5%)
• Never smoked	745 (76%)	942 (95%)	18 (62%)
Alcohol consumption			
• Habitual drinker	723 (73.8%)	976 (98.6%)	20 (69%)
• Non-Alcoholic	256 (26.2%)	13 (1.4%)	9 (31%)
Substance abuse			
• Current or past	8 (0.8%)	2 (0.2%)	3 (10.4%)
• Never	971 (99.2)	987 (99.8%)	26 (89.6%)
Fever	340 (34.7%)	65 (6.6%)	15 (51.2%)
Weight Loss	386 (39.3%)	272 (27.5%	15 (51.2%)
Loss of appetite	333 (34%)	269 (27.2%)	15 (51.2%
Lymphadenopathy	152 (15.5%)	237 (24%)	8 (27.6%)
Malignancy type			
• Non-Hodgkin's lymphoma		121 (12.4%)	13 (44.8%)
• Carcinoma Cervix		147 (15%)	6 (20.7%)
• Hodgkin's lymphoma		37 (3.4%)	4 (13.8%)
• Carcinoma Lung		41 (4.2%)	1 (3.4%)
• Carcinoma Gall bladder		24 (2.4%)	1 (3.4%)
• Sino-nasal SCC		15 (1.5%)	1 (3.4%)
• Skin SCC		2 (0.2%)	1 (3.4%)
• Adenocarcinoma Colon		31 (3.1%)	2 (6.8%)

Data is presented as mean ± standard deviation, Mean (Inter-quartile range); SCC: Squamous cell carcinoma

4. DISCUSSION

Our study suggests that approximately 2% of HIV patients had cancer, while 1% of cancer patients had HIV infection. AIDS-defining cancers remain more common than non-AIDS-defining cancers. In more developed countries with a higher life expectancy, non-AIDS-defining cancers predominate. It is expected that better coverage of ART, control of communicable diseases, and increased longevity would lead to an increase in non-AIDS-defining cancers and a decrease in AIDS-defining cancers [2, 26, 27].

The prevalence of HIV infection in cancer patients is very low, but it is approximately four times the national population (the national prevalence of HIV infection in India is 0.26%) [28]. In a similar report from Maharashtra, India, 3,832 patients were studied and the prevalence of HIV infection was only 1.2% [29].

AIDS-defining cancer such as NHL was around four times more common in patients with HIV compared to HIV-negative cancer patients. At the same center as the present study (AIIMS), a retrospective study analyzing malignancy in HIV patients during the initial years of ART (2005-2013) suggested a similar infrequent occurrence of malignancy in HIV, with NHL being the most common [30]. Most regional studies from India concur that NHL is the most common malignancy in HIV and KS is very rare [21-23, 29-33]. One of the reasons postulated is the low seroprevalence of HHV-8 in the Indian population [34]. However, a recent study by Munawwar *et al.* reported that 26% of 165 HIV-positive ART-naïve Indian men (90% heterosexual) had antibodies against HHV-8 [35]. The role of factors additional to HHV-8 in the pathogenesis of KS needs to be explored.

Diffuse large B-cell lymphoma is the most common subtype of NHL overall as well in the HIV population [2, 23, 24]. While EBV is commonly associated with immunodeficiency-related Hodgkin's lymphoma, its role in the pathogenesis of NHL in HIV varies, with most cases of primary CNS lymphoma expressing EBV proteins while rarely being associated with Burkitt lymphoma [36-38]. Outcomes of lymphoma have been worse in HIV-positive patients [39-41]. With effective chemotherapy and ART, there has been a better outcome reported with some studies showing similar outcomes as in HIV-negative patients [39, 42-44].

Patients with HIV are susceptible to chronic infection by oncogenic strains of HPV. In addition to causing cervical cancer, HPV also causes anal cancers and head and neck cancers [2, 45]. There is a high prevalence of HPV infection in HIV-infected women; almost one in four such patients have HPV co-infection with a high rate of intraepithelial neoplasia [46].

In this study, we observed a low prevalence of malignancies at the time of HIV diagnosis. We screened many successive patients at the ART and cancer center. It is yet to be observed whether HIV positive patients with malignancies have similar outcome as seronegative patients of the same stage. Drug interactions among chemotherapeutic agents and ART are also largely unknown. Though we followed HIV-cancer patients for one-year post-enrollment, stage of the diagnosed malignancy, treatment given and response is unknown. With effective ART and improvement in immunity it is expected that incidence of malignancy will be reduced, follow-up studies will help understand natural history of this disease.

HIV-related cancers are preventable through vaccination and early and highly active ART [2, 47, 48]. Screening of all HIV patients with clinical and radiological examinations should be conducted for early diagnosis and treatment of cancer. With this study, we have created a national HIV-cancer registry that will help to understand the spectrum of HIV-related malignancy in the hospital and community-based setting.

CONCLUSION

There is a low prevalence of cancer at the time of HIV diagnosis in North India. Similarly, HIV infection is rare in cancer patients. AIDS defining cancers remain most prevalent, while Kaposi's sarcoma is rare. Follow-up of these patients is required to see whether these patients have similar outcomes as compared to seronegative patients of the same stage.

LIST OF ABBREVIATIONS

ADC = AIDS defining cancers

AIDS = Acquired Immune Deficiency Syndrome

ART = Antiretroviral therapy

CD = Cluster of differentiation

CT = Computer tomography

EBV = Epstein-Barr Virus

ELISA = Enzyme-Linked Immunosorbent Assay

HHV-8 = Human Herpes Virus-8

HIV-1 = Human-immunodeficiency virus-1

HPV = Human Papilloma Virus

MRI = Magnetic Resonance Imaging

NHL = Non-Hodgkin's Lymphoma

PET = Positron Emission Tomography

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The protocol was approved by ethics committee of all India Institute of Medical Sciences, New Delhi, India.

HUMAN AND ANIMAL RIGHTS

No animals were used in this research. All humans research procedures followed were in accordance with the standards set forth in the Declaration of Helsinki principles of 1975, as revised in 2008 (http://www.wma.net/en/20 activities/10ethics/10helsinki/).

CONSENT FOR PUBLICATION

Written informed consent was taken from all subjects before participation in this study.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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REFERENCES

[1] Rubinstein PG, Aboulafia DM, Zloza A. Malignancies in HIV/AIDS: from epidemiology to therapeutic challenges. AIDS Lond Engl 2014; 28(4): 453-65.

[2] Yarchoan R, Uldrick TS. HIV-Associated cancers and related diseases. N Engl J Med 2018; 378(11): 1029-41.

[3] Shiels MS, Pfeiffer RM, Gail MH, *et al.* Cancer burden in the HIV-infected population in the United States. JNCI J Natl Cancer Inst 2011; 103(9): 753-62.

[4] Engels EA, Pfeiffer RM, Goedert JJ, *et al*. Trends in cancer risk among people with AIDS in the United States 1980-2002. AIDS 2006; 20(12): 1645-54.

[5] Long JL, Engels EA, Moore RD, Gebo KA. Incidence and outcomes of malignancy in the HAART era in an urban cohort of HIV-infected individuals. AIDS 2008; 22(4): 489-96.

[6] Crum-Cianflone N, Hullsiek KH, Marconi V, *et al.* Trends in the incidence of cancers among hiv-infected persons and the impact of antiretroviral therapy: A 20-year cohort study. AIDS 2009; 23(1): 41-50.

[7] Gill J, May M, Lewden C, Saag M, *at al*. Antiretroviral Therapy Cohort Collaboration. Causes of death in HIV-1-infected patients treated with antiretroviral therapy, 1996-2006: collaborative analysis of 13 HIV cohort studies. Clin Infect Dis Off Publ Infect Dis Soc Am. 2010; 50(10): 1387-96.

[8] Morlat P, Roussillon C, Henard S, *et al.* Causes of death among HIV-infected patients in France in 2010 (national survey): trends since 2000. AIDS Lond Engl 2014; 28(8): 1181-91.

[9] Vandenhende M-A, Roussillon C, Henard S, *et al*. Cancer-related causes of death among hiv-infected patients in France in 2010: evolution since 2000. PLOS ONE 2015; 10(6): e0129550.

[10] Centers for Disease Control (CDC). Update on acquired immune deficiency syndrome (AIDS)--United States. MMWR Morb Mortal Wkly Rep. 1982 Sep 24;31(37): 507-8, 513-4.

[11] Lanoy E, Dores GM, Madeleine MM, Toro JR, Fraumeni JF, Engels EA. Epidemiology of non-keratinocytic skin cancers among persons with acquired immunodeficiency syndrome in the U.S. AIDS Lond Engl 2009; 23(3): 385-93.

[12] Grulich AE, Li Y, McDonald AM, Correll PK, Law MG, Kaldor JM. Decreasing rates of Kaposi's sarcoma and non-Hodgkin's lymphoma in the era of potent combination anti-retroviral therapy. AIDS 2001; 15(5): 629-33.

[13] Deeken JF, Tjen-A-Looi A, Rudek MA, *et al.* The rising challenge of non-AIDS-defining cancers in HIV-infected patients. Clin Infect Dis Off Publ Infect Dis Soc Am 2012; 55(9): 1228-35.

[14] Powles T, Robinson D, Stebbing J, *et al.* Highly active antiretroviral therapy and the incidence of non-AIDS-defining cancers in people with HIV infection. J Clin Oncol Off J Am Soc Clin Oncol 2009; 27(6): 884-90.

[15] Chang Y, Cesarman E, Pessin MS, *et al.* Identification of herpesvirus-like DNA sequences in AIDS-associated Kaposi's sarcoma. Science 1994; 266(5192): 1865-69.

[16] Frisch M, Biggar RJ, Goedert JJ. Human papillomavirus-associated cancers in patients with human immunodeficiency virus infection and acquired immunodeficiency syndrome. J Natl Cancer Inst 2000; 92(18): 1500-10.

[17] MacMahon EM, Glass JD, Hayward SD, *et al.* Epstein-Barr virus in AIDS-related primary central nervous system lymphoma. Lancet 1991; 338(8773): 969-73.

[18] Hamilton-Dutoit SJ, Raphael M, Audouin J, *et al.* In situ demonstration of Epstein-Barr virus small RNAs (EBER 1) in acquired immunodeficiency syndrome-related lymphomas: correlation with tumor morphology and primary site. Blood 1993; 82(2): 619-24.

[19] HIV/AIDS. World Health Organization. [cited 2018 Apr 30]. Available from: http://www.who.int/news-room/fact-sheets/detail/hiv-aids

[20] UNAIDS, India. [cited 2018 Apr 30]. Available from: http://www.unaids.org/en/regionscountries/countries/india.

[21] Paul TR, Uppin MS, Uppin SG, *et al.* Spectrum of malignancies in human immunodeficiency virus – positive patients at a tertiary care centre in South India. Indian J Cancer 2014; 51(4): 459.

[22] Dhir AA, Sawant S, Dikshit RP, *et al.* Spectrum of HIV/AIDS related cancers in India. Cancer Causes Control 2008; 19(2): 147-53.

[23] Sachdeva RK, Sharma A, Singh S, Varma S. Spectrum of AIDS defining & non-AIDS defining malignancies in north India. Indian J Med Res 2016; 143(Suppl 1): S129-35.

[24] Agarwal B, Ramanathan U, Lokeshwas N, *et al.* Lymphoid neoplasms in HIV-positive individuals in India. J Acquir Immune Defic Syndr 2002; 29(2): 181-3.

[25] OM - Revised Guidelines for ART | National AIDS Control Organization | MoHFW | GoI [Internet]. [cited 2018 Apr 30]. Available from: http://naco.gov.in/om-revised-guidelines-art.

[26] Crum-Cianflone N, Hullsiek KH, Marconi V, *et al.* Trends in the incidence of cancers among hiv-infected persons and the impact of antiretroviral therapy: a 20-year cohort study. AIDS Lond Engl 2009; 23(1): 41-50.

[27] Grulich AE, Li Y, McDonald AM, Correll PK, Law MG, Kaldor JM. Decreasing rates of Kaposi's sarcoma and non-Hodgkin's lymphoma in the era of potent combination anti-retroviral therapy. AIDS Lond Engl 2001; 15(5): 629-33.

[28] HIV Facts & Figures | National AIDS Control Organization | MoHFW | GoI. [cited 2018 May 4]. Available from: http://naco.gov.in/hiv-facts-figures.

[29] Phatak UA, Joshi R, Badakh DK, Gosavi VS, Phatak JU, Jagdale RV. AIDS-associated cancers: an emerging challenge. J Assoc Physicians India 2010; 58: 159-62.

[30] Sharma S, Soneja M, Ranjan S. Malignancies in human immunodeficiency virus infected patients in India: Initial experience in the HAART era. Indian J Med Res 2015; 142(5): 563.

[31] Venkatesh KK, Saghayam S, Devaleenal B, *et al.* Spectrum of malignancies among HIV-infected patients in South India. Indian J Cancer 2012; 49(1): 176.

[32] Prem S, Narayanan G, Puthuveettil J, K J, K V. Spectrum of HIV/AIDS-associated cancers in south India. J Clin Oncol 2014; 32(15_suppl): e12534-e12534.

[33] Sharma A, Bajpai J, Raina V, Mohanti BK. HIV-associated non-Hodgkin's lymphoma: experience from a regional cancer center. Indian J Cancer 2010; 47(1): 35-9.

[34] Ablashi D, Chatlynne L, Cooper H, Thomas D, Yadav M, Norhanom AW, *et al.* Seroprevalence of human herpesvirus-8 (HHV-8) in countries of Southeast Asia compared to the USA, the Caribbean and Africa. Br J Cancer 1999; 81(5): 893-7.

[35] Munawwar A, Sharma SK, Gupta S, Singh S. Seroprevalence and determinants of kaposi sarcoma-associated human herpesvirus 8 in indian hiv-infected males. AIDS Res Hum Retroviruses 2014; 30(12): 1192-6.

[36] MacMahon EM, Glass JD, Hayward SD, *et al.* Epstein-Barr virus in AIDS-related primary central nervous system lymphoma. Lancet Lond Engl 1991; 338(8773): 969-73.

[37] Uldrick TS, Little RF. How i treat classical hodgkin lymphoma in patients infected with human immunodeficiency virus. Blood 2015; 125(8): 1226-35; 1355.

[38] Hamilton-Dutoit SJ, Raphael M, Audouin J, *et al.* In situ demonstration of Epstein-Barr virus small RNAs (EBER 1) in acquired immunodeficiency syndrome-related lymphomas: correlation with tumor morphology and primary site. Blood 1993; 82(2): 619-24.

[39] Barta SK, Samuel MS, Xue X, Wang D, Lee JY, Mounier N, *et al.* Changes in the influence of lymphoma- and HIV-specific factors on outcomes in AIDS-related non-Hodgkin lymphoma. Ann Oncol 2015; 26(5): 958-66.

[40] Cingolani A, Lepri AC, Teofili L, *et al.* Survival and predictors of death in people with HIV-associated lymphoma compared to those with a diagnosis of lymphoma in general population. PLOS ONE 2017; 12(10): e0186549.

[41] Gopal S, Patel MR, Yanik EL, *et al.* Temporal trends in presentation and survival for hiv-associated lymphoma in the antiretroviral therapy era. JNCI J Natl Cancer Inst 2013; 105(16): 1221-9.

[42] Coutinho R, Pria AD, Gandhi S, *et al.* HIV status does not impair the outcome of patients diagnosed with diffuse large B-cell lymphoma treated with R-CHOP in the cART era: AIDS. 2014 ; 28(5): 689-97.

[43] Hleyhel M, Belot A, Bouvier A-M, *et al.* Trends in survival after cancer diagnosis among HIV-infected individuals between 1992 and 2009. Results from the FHDH-ANRS CO4 cohort. Int J Cancer 2015; 137(10): 2443-53.

[44] Besson C, Lancar R, Prevot S, *et al.* Outcomes for Hiv-associated diffuse large B-cell lymphoma in the modern combined antiretroviral therapy era. Aids 2017; 31(18): 2493-501.

[45] Williams AB, Darragh TM, Vranizan K, Ochia C, Moss AR, Palefsky JM. Anal and cervical human papillomavirus infection and risk of anal and cervical epithelial abnormalities in human immunodeficiency virus-infected women. Obstet Gynecol 1994; 83(2): 205-11.

[46] Chakravarty J, Chourasia A, Thakur M, Singh A, Sundar S, Agrawal N. Prevalence of human papillomavirus infection & cervical abnormalities in HIV-positive women in eastern India. Indian J Med Res 2016; 143(1): 79.

[47] Goncalves PH, Montezuma-Rusca JM, Yarchoan R, Uldrick TS. Cancer prevention in HIV-infected populations. Semin Oncol 2016 Feb; 43(1): 173-88.

[48] Lowy DR, Schiller JT. Prophylactic human papillomavirus vaccines. J Clin Invest 2006; 116(5): 1167-73.