

Observation of Hematological Profile in HIV Positive Patients Before and After Initiation of Highly Active Anti-Retroviral Therapy.

¹Dr. Siddharth Kapoor, ²Dr. Parijat Mishra

³Dr. Sandeep M Horo, ⁴Dr. J K Mitra

¹Registrar, Department of Medicine, Rajendra Institute of Medical Sciences, Ranchi

²Intern, Rajendra Institute of Medical Sciences, Ranchi

³Senior Resident, Department of Medicine, Rajendra Institute of Medical Sciences, Ranchi

⁴H.O.D., Department of Medicine, Rajendra Institute of Medical Sciences, Ranchi

Corresponding Author – Dr. Siddharth Kapoor

Date of Submission: 29-05-2019

Date of acceptance: 15-06-2019

I. Introduction

Human immunodeficiency virus (HIV) is the causative agent of Acquired Immunodeficiency Syndrome (AIDS). Due to the large scale of morbidity & mortality it causes, HIV is fast becoming a major threat in developing/third world countries (1).

HIV is characterized by progressive damage to the body's immune system which results in the development of many opportunistic infections and complications. The hematological complications of HIV-infected patients include anaemia, neutropenia, lymphopenia and thrombocytopenia. Anemia is the most commonly encountered hematological abnormalities in HIV patients (2).

Approximately 15% of asymptomatic subjects infected with HIV have mild anemia. The prevalence of anemia increases to 30% to 40% in those with early disease and 75% to 90% in those with AIDS.(3) These abnormalities are frequently multifactorial; however, an important role in their pathogenesis has been ascribed to a defective hematopoiesis.(4)

ART helps the body's immune system recover from the damage caused by infection with HIV. Different classes of Antiretroviral drugs act at different stages of HIV cycle. Combination of several, typically three or four drugs are known as Highly Active Anti Retroviral Therapy (HAART), which create multiple obstacles to HIV replication, thereby keeping the number low and reducing the possibility of a superior mutation. HAART produces profound suppression of HIV replication, substantial increase in CD4+ T cells and partial reconstitution of the immune system. All of these result in significant declines of the morbidity and mortality in HIV/AIDS patients. Immune reconstitution in AIDS patients after HAART has been reported in several countries (5, 6, 7 and 8).

In this study, we analyze the hematological parameters of HIV positive patients before and after 6 & 12 months of initiation of HAART.

II. Materials and methods

This prospective study was conducted to assess hematological profile among HIV infected individuals after initiation of Highly Active Anti Retroviral Therapy (HAART) at ART clinic of Rajendra Institute of Medical Sciences, Ranchi. Patients detected to be HIV positive as per WHO criteria attending to Department of Medicine/ART Centre, Rajendra Institute of Medical Sciences(RIMS), Ranchi, during the period of January 2012 to September 2013 were taken up for the study. The study participants were HIV infected individuals who had started HAART (defined as two or more antiretroviral drugs for at least 6 months), by WHO clinical and immunological criteria (9), and who had TLC, CD4 + T cell, Hemoglobin(Hb) and Absolute Neutrophil Count and Absolute Lymphocyte Count taken at the time of ART initiation and at 6 & 12 months after initiation of the treatment. Patients with previously known hematological disorders or congenital hematological disorders were excluded from the study. Participants' demographic variables, prophylaxis taken and type of ART regimen, hematological values were carefully extracted from ART log book and patient follow up cards by using a NACO standardized Data Extraction format from the baseline (January 2012). All covariates for each patient were collected at 0 month (baseline), 6 month and 12 month following initiation of HAART. Anemia is defined as hemoglobin < 13 gm/dl for men and < 12 gm/dl for women (10). Leucopenia is defined as TLC count less

than 3,000 cells/ μ l (11). Neutropenia is defined as absolute neutrophil count (ABLN) less than 1700 cells/cumm. Lymphopenia is defined as absolute lymphocyte count (ABLL) less than 1500 cells/cumm. Mild anemia is defined as hemoglobin values of 10-12gm/dl for women and 10-13 gm/dl for men, moderate anemia is hemoglobin values of 8-9.9 gm/dl and severe anemia defined as hemoglobin values less than 8 gm/dl (12). Immunosuppression is defined as a CD4+ T cell count <200 cells/ μ l (13).

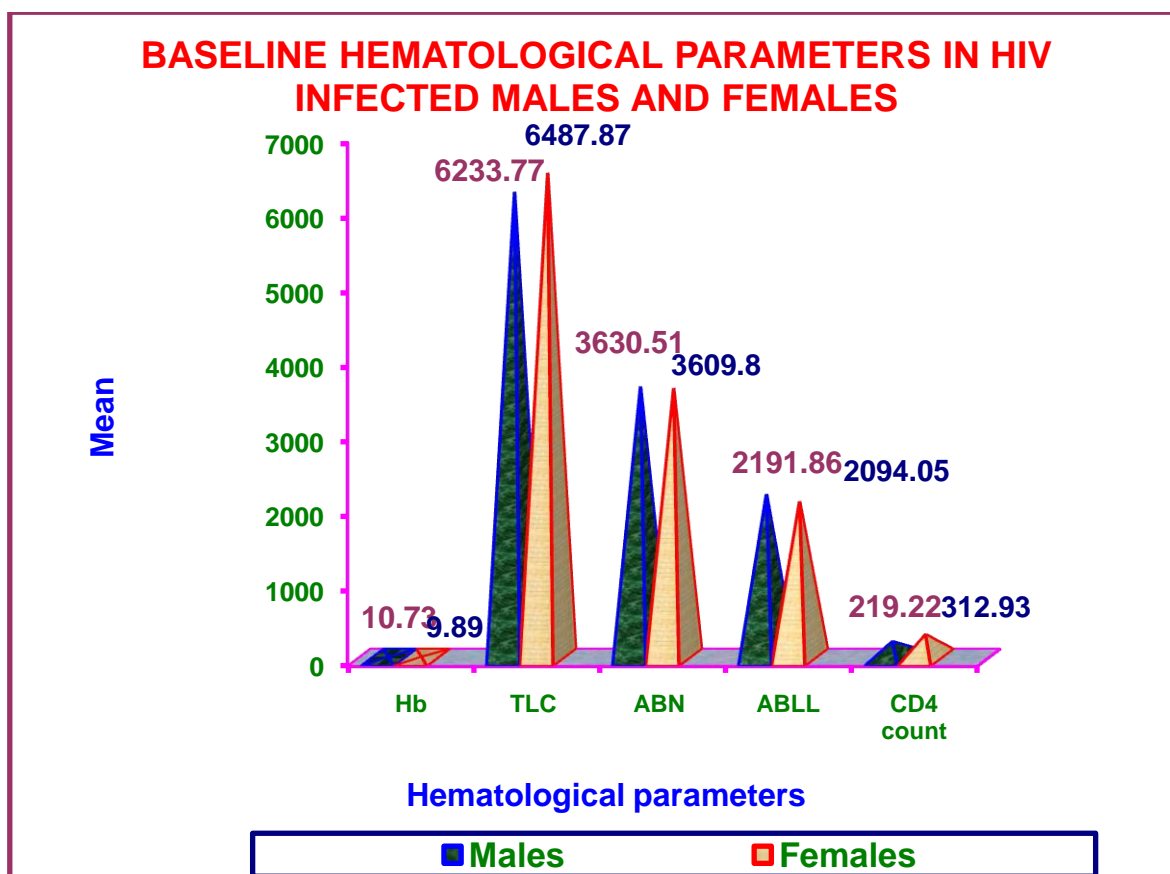
Data collected through a standardized questionnaire were entered into Excel spread sheet and transported into and analyzed by Medcalc version 11.2.1.0. Values are presented as mean and \pm SD as appropriate. A P-value <0.05 was considered statistically significant.

III. Results

In this study the hematological profile was studied in 100 patients with HIV infection and observations were recorded in a tabulated manner, the data were statistically analysed. Of the 100 patients studied, 53(53%) were males as against 47(47%) females with a sex ratio of 1.12:1.

TABLE – 1: Hematological Parameters In Hiv Infected Males And Females Prior To Haart

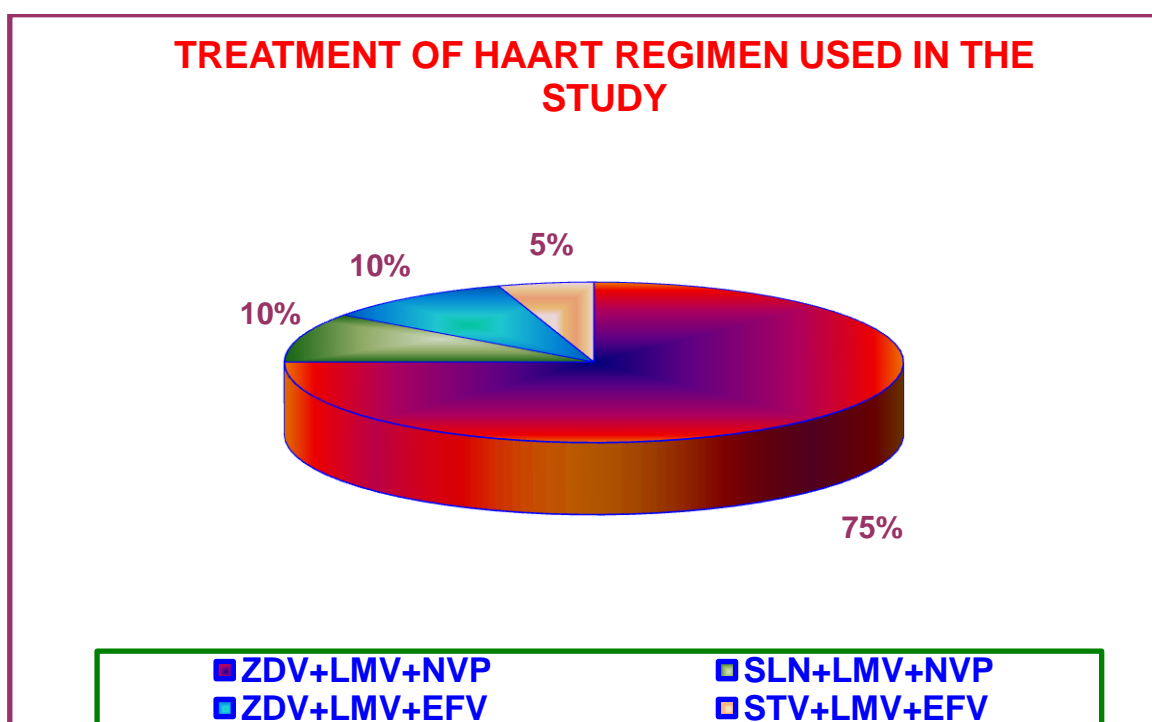
Hematological parameters	Total (n=100)		Male (n=53)		Female (n=47)		P value
	Mean	SD	Mean	SD	Mean	SD	
Hb (gm%)	10.33	1.63	10.73	1.48	9.89	1.69	0.0094
Range (gm%)	6-14.4		7.0-14.4		6-13.5		
TLC (cell/cumm)	6353.20	2339.94	6233.77	2176.81	6487.87	2528.31	0.590
Range (cell/cumm)	1700-12100		1800-12100		1700-11750		
Absolute Neutrophils count (cell/cumm)	3620.78	1640.23	3630.51	1603.49	3609.80	1698.04	0.948
Range (cell/cumm)	194-7844		194-7844		578-7560		
Absolute Lymphocytes count (cell/cumm)	2145.89	952.93	2191.86	1066.96	2094.05	813.80	0.610
Range (cell/cumm)	329.00-5350.80		329.00-5350.80		765.00-3857.00		
CD4 count	263.27	165.17	219.22	131.84	312.93	185.23	0.0041
Range	1.00-905		21.00-508		1.00-905		



The baseline (pre-HAART) data shows that the mean Hb is 10.33 ± 1.63 g/dL. In case of males, Hb was 10.73 ± 1.48 g/dL, whereas in females, mean was 9.89 ± 1.69 g/dL. The TLC shows a mean of 6353.20 ± 2339.94 cell/cumm IQR(1700-12100) cell/cumm, of which males show a mean of 6233.77 ± 2176.81 cell/cumm IQR(1800-12100)cell/cumm and females show a mean of 6487.87 ± 2528.31 cell/cumm IQR(1700-11750)cell/cumm. The ABN shows a mean of 3620.78 ± 1640.23 out of which males have a mean of 3630.51 ± 1603.49 cell/cumm and females have mean 3609.80 ± 1698.04 cell/cumm. The ABLL shows a mean overall 2145.89 ± 952.93 cell/cumm out of which males have mean 2191.86 ± 1066.96 cell/cumm and females have mean 2094.05 ± 813.80 cell/cumm. The CD4 count overall was 263.27 ± 165.17 /dL out of which males show mean 219.22 ± 131.84 /dL and females have mean 312.93 ± 185.23 /dL. The significant values reach only for Hb(0.0094) and CD4(0.0041).

TABLE – 2: Treatment of Haart Regimen Used In The Study

Treatment regimen	Number (n=100)	Percentage
ZDV+LMV+NVP	75	75
SLN+LMV+NVP	10	10
ZDV+LMV+EFV	10	10
STV+LMV+EFV	5	5



Above table shows that ZDV+LMV+NVP combination was used in 75% of cases followed by SLN+LMV+NVP & ZDV+LMV+EFV 10% of each. STV+LMV+EFV was used in 5% cases.

Table – 3: Comparison of Hematological Parameters Between Baseline And 6 Months After Initiation Of Haart

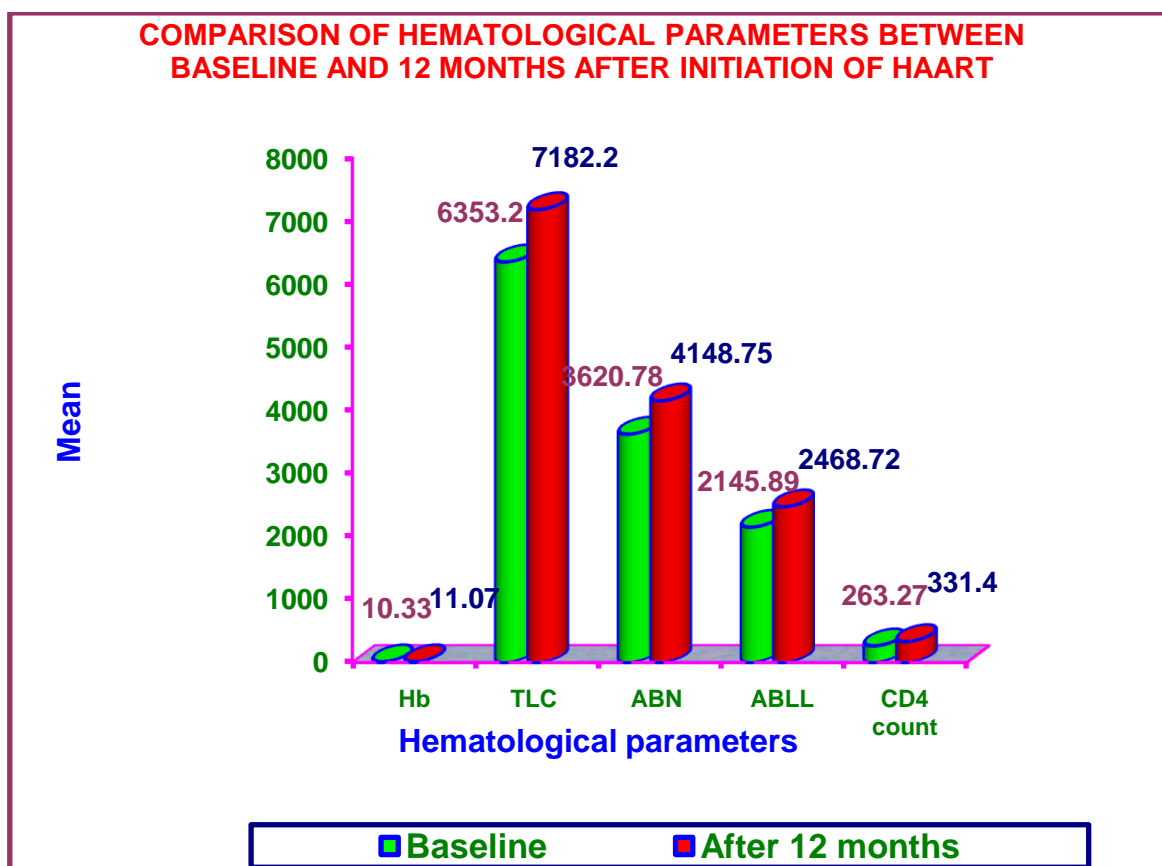
Hematological parameters	Baseline (n=100)		After 6 months (n=100)		P value
	Number±SD	Range	Number±SD	Range	
Hb%	10.33±1.63	6-14.4	10.43±1.61	6.8-14.4	0.663
TLC (cell/cumm)	6353.20±2339.94	1700-12100	6681.50±1597.40	2300-11250	0.247
Absolute Neutrophil count (cell/cumm)	3620.78±1640.23	194-7844	3651.19±1241.37	306-7844	0.882
Absolute Lymphocytes count (cell/cumm)	2145.89±952.93	329.00-5350.80	2029.89±618.09	700.00-4275.00	0.308
CD4 count (cell/cumm)	263.27±165.17	1.00-905	287.37±134.14	66.00-644.00	0.258

The mean hemoglobin at baseline (prior to HAART) is 10.33 ± 1.63 g/dL which after 6 months of HAART is 10.43 ± 1.61 g/dL ($p=0.663$). The TLC at baseline were 6353.20 ± 2339.94 cell/cumm which after 6 months is 6681.50 ± 1597.40 cell/cumm ($p=0.247$). The ABLN at baseline and after 6 months show 3620.78

± 1640.23 cell/cumm and 3651.19 ± 1241.37 cell/cumm respectively ($p=0.882$). None of the values were significant.

Table – 4: Comparison of Hematological Parameters between Baseline And 12 Months After Initiation Of Haart

Hematological parameters	Baseline (n=100)		After 12 months (n=100)		P value
	Number \pm SD	Range	Number \pm SD	Range	
Hb (gm%)	10.33 \pm 1.63	6-14.4	11.07 \pm 1.66	6.4-16.6	0.001
TLC (cell/cumm)	6353.20 \pm 2339.94	1700-12100	7182.25 \pm 2192.94	1125-13500	0.010
Absolute Neutrophil count (cell/cumm)	3620.78 \pm 1640.23	194-7844	4148.75 \pm 1966.62	247.50-10395	0.040
Absolute Lymphocytes count (cell/cumm)	2145.89 \pm 952.93	329.00-5350.80	2468.72 \pm 985.42	256-6664	0.0195
CD4 count	263.27 \pm 165.17	1.00-905	331.40 \pm 140.99	72-737	0.002



The table shows Hb% at baseline is 10.33 ± 1.63 g/dL prior to HAART and after 12 month is 11.07 ± 1.66 g/dL ($p=0.001$). The TLC at baseline and after 12 months is 6353.20 ± 2339.94 cell/cumm and 7182.25 ± 2192.94 cell/cumm respectively ($p=0.010$). The ABLN count at baseline and after 12 months of HAART is 3620.78 ± 1640.23 cell/cumm and 4148.75 ± 1966.62 cell/cumm respectively ($p=0.040$). The ABLL count at baseline and after 12 months of HAART is 2145.89 ± 952.93 cell/cumm and 2468.72 ± 985.42 cell/cumm respectively ($p=0.0195$). The CD4 count at baseline and after 12 months of HAART are 263.27 ± 165.17 /dL and 331.40 ± 140.99 /dL respectively ($p=0.002$).

IV. Discussion

The result of the data analysis obtained shows a predominance of males amongst 100 patients that is males constituted 53% ($n=53$). Hematological parameters did not show statistically significant difference between males and females, except mean haemoglobin ($p < 0.009$), at the initiation of HAART.

HIV infection may lead to anemia in many ways; some of them are changes in cytokine production, decreased erythropoietin concentrations, opportunistic infectious agents (5). The present study has shown that from the total of 53 males; 52 (98.11%) and from the total of 47 females; 42 (89.36%) were anemic. In another

study conducted in India, anemia was seen in 65.5% of patients (14). Antiretroviral therapy decreases the prevalence of anemia in HIV infected patients and it is essential for the hemoglobin restoration of these patients. The present study revealed that the mean hemoglobin was 10.33 gm% IQR (6.0-14.4) gm/dl and 10.43 gm% IQR (6.8-14.4) gm% at the baseline and after 6 month initiation of HAART respectively ($p < 0.663$).

The present study revealed that the mean CD4+ T cells count at the baseline for 100 patients was 263.27 cells/cumm IQR (1-905) cells/cumm and after 6 month initiation of HAART, increased to 287.37 cells/cumm IQR (66-644) cells/cumm ($p = 0.258$). Our study also showed statistically significant change in CD4+T count after 12 months of follow-up of HAART ($p = 0.002$). Our result is in agreement with the result of a study conducted in China (5).

In our study, the mean white blood cell count at the baseline was 6353.20 cells/cumm IQR (1700-12100) cells/cumm and after 6 month initiation of HAART, increased to 6681.50 IQR (2300-11250) cells/cumm ($P = 0.247$). Antiretroviral drugs described improvement of leucopenia.

The present study shows absolute neutrophil (ABNL) count at baseline was 3620.78 cells/cumm IQR (194-7844) cells/cumm which after 6 months increases to 3651.19 cells/cumm IQR (306-7844) cells/cumm which was statistically not significant ($p = 0.882$). After follow up of 12 months the ABLN rises significantly to 4148.75 cells/cumm IQR (247.5-10395) cells/cumm ($p = 0.040$).

Our study shows absolute lymphocyte count (ABLL) at baseline 2145.89 cells/cumm (IQR (329-5350) cells/cumm which after a follow up of 6 and 12 months was 2029.89 cells/cumm IQR (700-4275) cells/cumm and 2468.72 IQR (256-6664) cells/cumm. The difference was not statistically significant for 6 months ($p = 0.308$) but it was significant after 12 months HAART ($p = 0.0195$).

The mean changes of WBC count from baseline were not significant at 6 month of ART but showed significant change as the treatment continued. Trend of hematological parameters of patients following antiretroviral treatment indicated that the parameters increased at 12 month of ART significantly. HAART results in immunologic improvement, even among persons with low pre-therapy CD4+ lymphocyte counts.

V. Conclusion

On the basis of above observation made in the prospective cohort study, it can be concluded that hematological disorders are very common in HIV patients, and anemia is a very important and common presentation in this group. HAART produces a definitive improvement of hematological parameters such as haemoglobin, absolute neutrophil count, absolute lymphocyte count, total count and CD4 count. The significant improvement in CD4 cells and hemoglobin was observed after six months of HAART. Improvement in TLC, absolute neutrophil count, absolute lymphocyte count was observed after twelve months of HAART. It can be concluded that in PEOPLE LIVING WITH HIV/AIDS (PLWHA), HAART is useful for modifying the morbidity and mortality.

References

- [1]. Rombauts B. Farmaceutische Microbiologie (met inbegrip van de farmaceutische technologie van steriele geneesmiddelen). *Cursus 1 ste graad apotheker VUB* 1997;11:14-16.
- [2]. Spivak JL, Bender BS, Quin TC. Hematological abnormalities in the acquired immune deficiency syndrome. *Am J Med* 1984;77:224-8.
- [3]. Zauli G, Davis BR, Re MC. Fat protein stimulates production of transforming growth factor – beta-1 by the bone marrow macrophages: A potential mechanism for human immunodeficiency virus-1-induced hematopoietic suppression. *Blood* 1992;80:3036-43.
- [4]. Zon LI, Groopman JE. Hematological manifestations of human immune deficiency virus (HIV). *Semin Hematol* 1988;25:208.
- [5]. Castella A, Croxson T, Midvan D. The bone marrow in AIDS. A histologic, hematological and microbiologic study. *Am J Clin Pathol* 1985;84:425-32.
- [6]. Ensoli B. Pathogenesis of AIDS-associated Kaposi sarcoma. *Hematol Onco Clin North Am* 1991;5:281.
- [7]. Reynolds P, Saunders LD, Leyfski ME, Lemp GF. The spectrum of acquired immunodeficiency syndrome (AIDS) – associated malignancies in San Francisco, 1980-1987. *Am J Epidemiol* 1993;137-49.
- [8]. Lytner DW, Bryant J, Thackeray R. Incidence of immunodeficiency virus related and non-related malignancies in a large cohort of homosexual men. *J Clin Oncol* 1995; 13:2540-46.
- [9]. Garcia JV, Miller AD. Down regulation of cell surface CD4 by nef. *Res Virol* 1992;143:52-5.
- [10]. Franchini G, Bosch ML. Genetic relatedness of the human immunodeficiency viruses type 1 and 2 (HIV-1, HIV-2) and the simian immunodeficiency virus (SIV). *Ann NY Acad Sci* 1989;554:81-7.
- [11]. Heinzinger NK, Bukinsky MI, Haggerty SA. The Vpr protein of human immunodeficiency virus type 1- influences nuclear localization of viral nucleic acids in nondividing host cells. *Proc Natl Acad Sci USA* 1994;91:7311-15.
- [12]. Lewis P, Hensel M, Emerman M. Human immunodeficiency virus infection of cells arrested in the cell cycle. *EMBO J* 1992;11:3053-8.
- [13]. Tapolsky LM., De Rocquigny H, Van Gent D. Interactions between HIV-1 nucleocapsid protein and viral DNA may have important functions in the viral life cycle. *Nucleic Acids Res* 1993;21:831-9.

Dr. Siddharth Kapoor. "Observation of Hematological Profile in HIV Positive Patients Before and After Initiation of Highly Active Anti-Retroviral Therapy." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, vol. 18, no. 6, 2019, pp 16-20.