A STUDY OF HAEMATOLOGICAL MANIFESTATIONS IN HUMAN IMMUNE DEFICIENCY VIRUS POSITIVE PATIENTS BEFORE AND AFTER ANTIRETROVIRAL THERAPY

Madhu Balla[1], Vijay Kumar[2]

[1]Postgraduate, Department of Pathology, Government Medical College, Jammu, Jammu and Kashmir.
[2]Registrar, Department of Internal Medicine, Government Medical College, Jammu, Jammu and Kashmir.

ABSTRACT

BACKGROUND

HIV infection is a multisystem disease and haematological abnormalities are among the most common complications of HIV. HIV associated haematological abnormalities seem to be dependent on the level of virus replication, as these abnormalities are severe in late stage AIDS patients with high viremia. These abnormalities reflect the underlying immune status and may be prevented or corrected by use of highly active antiretroviral therapy (HAART).

METHODS

One hundred HIV positive patients, symptomatic as well asymptomatic, diagnosed by enzyme-linked immunosorbent assay (ELISA) method according to the National AIDS Control Organization (NACO) guidelines were included. Complete haematological profile was recorded. The haematological parameters of each patient were evaluated at 0-, 6- and 12-months following initiation of HAART.

RESULTS

Out of 100 patients included in this study, 58% (58) were males and 42% (42) were females with the sex ratio of 1.38:1. The haematological profiles were presented as mean ± standard deviation. A p value of 0.05 was considered statistically significant. There was a significant improvement in CD4 cells, haemoglobin, red cell count and haematocrit and platelet counts after 6 months and 12 months of therapy. Improvement in total count, absolute neutrophil count and absolute lymphocyte count was observed after 12 months of HAART.

CONCLUSIONS

This study shows that there was improvement in all parameters in these patients and also in the stage of disease when they were followed for one year. So, regular follow up and compliance of patient is of utmost importance in checking the progress of disease as well as ensuring better quality of life. It can be concluded that in people living with HIV/AIDS, HAART is useful for modifying the mortality and morbidity.

KEYWORDS

HIV, CD4 Counts, Haematological Parameters, Anemia, Leukopenia, Thrombocytopenia.

HOW TO CITE THIS ARTICLE: Balla M, Kumar V. A study of haematological manifestations in human immune deficiency virus positive patients before and after antiretroviral therapy. J. Evid. Based Med. Healthc. 2019; 6(21), 1537-1541. DOI: 10.18410/jebmh/2019/310

BACKGROUND

Human Immunodeficiency Virus belongs to family of human retroviruses. HIV infection is marked by progressive decrease in the number of circulating CD_4 + T helper cells, which over a period of years leads to immunological decline and death due to opportunistic infections and neoplasms. HIV causes the Acquired Immunodeficiency syndrome (AIDS)[1] (WHO, 1991). AIDS is either characterized by the presence of a particular opportunistic infection or the CD_4+ T lymphocyte count being <200/mm^3 or a combination of both (Kasthuri AS et al., 2006)[2] HIV infection is a multisystem disease and haematological abnormalities are among the most common complications of HIV (Dhurve SA et al., 2014).[3] Haematological abnormalities such as impaired haematopoiesis, immune and non-immune mediated cytopenia and altered coagulation have been described in patients with HIV infection /AIDS (Kasthuri AS et al., 2006).[2]

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 antiretroviral therapy (HAART).These drugs must be taken in combination in order to have lasting effect (Amegor O et al.,2009).[4] Immune reconstitution in AIDS patients after HAART has been reported in several countries (Dai yi et al;[5] WKBA O et al;[6] Huruy K et al[7]).

Aims and Objectives

The aim of the study was to evaluate the various haematological parameters in HIV patients and to compare

Financial or Other, Competing Interest: None.
Submission 05-05-2019, Peer Review 08-05-2019,
Acceptance 20-05-2019, Published 27-05-2019.
Corresponding Author:
Dr. Vijay Kumar,
R/o, Doulah Tehsil,
Bani Kathua- 184206,
Jammu and Kashmir.
E-mail: drvijaygmc97@gmail.com
DOI: 10.18410/jebmh/2019/310

the mean differences of selected haematological profile between baseline, after 6 months and 12 months.

METHODS

The present study was a one-year observational study conducted from 1st October 2016 to 31st September 2017 in Haematology wing of Postgraduate Department of Pathology Government Medical College, Jammu. One hundred patients, seropositive for HIV by ELISA were included in the study. Ethical clearance from the institutional ethical committee was obtained. These patients were observed in detail and complete data of each patient was prepared. Complete haematological evaluation including CD_4 count was done. Blood collected in a sterile EDTA containing tube and processed following our established laboratory protocol and universal precautions as per guideline of National AIDS Control Organisation (NACO, India). Written informed consent was taken from all.

Inclusion Criteria

This was a prospective study and was conducted on newly diagnosed patients of HIV who were attending HIV/AIDS clinic.

Exclusion Criteria

- Pregnant women.
- Patients under 16 years of age.
- Patients of malignancy not related to HIV disease.
- Patients not given consent.

Statistical Methods

Descriptive statistics were expressed as mean ± standard deviation and results on categorical measurements as numbers (%). Statistical analysis was done using SPSS 16.0 version, P <0.05 statistically significant.

RESULTS

Demographic Data: Out of 100 patients included in this study, 58% (58) were males against 42% (42) females with the sex ratio of 1.38:1. Most of the males (50%) and females (45%) were in the age group of 31-40 years. Minimum age of the patient was 19 years and maximum age was 61 years. Most common age group was 21-40 years with mean age of 36.59 ± 9.12 (Table -1)

Age Distribution (Years)	Number of Patients (%)	
	Male (n=58)	Female (n=42)
≤20	1 (1.72)	3 (7.14)
21-30	8 (13.79)	15 (35.71)
31-40	29 (50.00)	19 (45.24)
41-50	11 (18.97)	2 (4.76)
51-60	8 (13.79)	3 (7.14)
>60	1 (1.72)	0 (0.00)
Mean Age ± SD	36.59 ± 9.12	
p Value	<0.0001	

Table 1. Distribution of Patients According to Age and Sex

Table 2 shows the mean haemoglobin which at baseline (at the time of presentation) was 9.94 ± 1.76, after 6 months was 10.73 ± 1.60 and after 12 months was 11.61 ± 1.52 with p value of <0.0001 which shows that there was a statically highly significant increase in mean to 11.61 ± 1.52. Other parameters that showed statically significant difference in mean after 12 months of therapy was RBC count (p value <0.0001) and platelet count. However p value for total leukocyte count, absolute neutrophil count, absolute lymphocyte count was not statistically significant.

Haematological Parameters	Mean ± Standard Deviation			p Value
	Baseline* (n=100)	After 6 Months (n=100)	After 12 Months (n=97)	
Hb (gm/dl)	9.94 ± 1.76	10.73 ± 1.60	11.61 ± 1.52	<0.0001
RBC Count (m/mm^3)	3.59 ± 0.54	3.79 ± 0.56	4.00 ± 0.58	<0.0001
TLC (mm^3)	6893.00 ± 2174.61	6697.00 ± 1788.60	7271.13 ± 2028.18	0.126
Neutrophils	64.76 ± 6.89	63.53 ± 7.12	63.99 ± 8.02	0.490
Lymphocytes	30.87 ± 6.42	31.97 ± 7.23	31.24 ± 7.42	0.532
Monocytes	2.08 ± 0.86	2.3 ± 0.67	2.45 ± 1.03	0.010
Eosinophils	2.25 ± 1.09	2.21 ± 0.86	2.33 ± 1.04	0.692
ANC (cells/µL)	4494.88 ± 1785.21	4282.45 ± 1468.88	4727.79 ± 1687.08	0.169
ALC (cells/µL)	2087.68 ± 662.87	2095.72 ± 549.94	2217.37 ± 682.35	0.277
Platelets (L/ mm3)	1.86 ± 0.43	1.99 ± 0.51	2.04 ± 0.63	0.050

Table 2. Haematological Parameters in HIV Infected Patients

*at the time of presentation.

Statistically significant increase in mean haematocrit was also seen after 12 months of therapy (p value=0.001). Mean erythrocyte sedimentation rate at base line was 22.75 ± 22.28 (prior to HAART) which after 6 months of therapy was 17.31 ± 13.39 and after 12 months of therapy, there was a statically significant decrease in mean to 13.38 ± 13.38 with p value of 0.0001 (Table-3). MCV and MCH also showed corresponding increase in mean with the follow up period but it was not statically significant.

Haematological Parameters	Mean ± Standard Deviation			p Value
	Baseline (n=100)	After 6 Months (n=100)	After 12 Months (n=97)	
ESR (mm/hr)	22.75 ± 22.28	17.31 ± 13.39	13.38 ± 13.38	0.0001
MCV (fl)	83.91 ± 12.62	84.90 ± 9.73	86.30 ± 7.55	0.256
MCH (pg)	26.95 ± 3.89	27.38 ± 3.33	28.01 ± 2.75	0.086
MCHC (g/dl)	30.76 ± 1.71	31.24 ± 1.70	31.84 ± 1.71	0.001
HCT	36.21 ± 4.09	37.31 ± 4.31	38.51 ± 4.19	0.001

Table 3. Haematological Parameters in HIV Infected Patients at Different Time Periods

Anaemia was the most common haematological abnormality at the time of presentation in these patients. Among the total of 100 cases, 93 (93%) cases had anaemia and 7 (7%) cases had normal haemoglobin at the time of presentation.

After 6 months of therapy anaemia was seen in 87% of cases which reduced to 76% after 12 months of therapy. Anaemia was graded based on haemoglobin level into mild, moderate and severe anaemia (Table-4). Mild anaemia was seen in 26% of males (Hb range 10-13 gm) and 15% of females (Hb range 10-12 gm) at the time of presentation, 28% males and 19% of females after 6 month of therapy and 34% of males and 18% of females were having mild anaemia after 12 months of therapy. Moderate anaemia (Hb range 7.0-9.9) was seen in 46% of patients at the time of presentation which reduced to 28% cases after 6 months of therapy and 10.31% cases at 12 months of therapy. Severe anaemia (Hb <7 gm) was seen in 6% of cases at the time of presentation which to 1% case after 6 months of therapy and no patient had severe anaemia after 12 months of therapy. Relation of anaemia with the duration of therapy was statistically significant (p<0.0001)

Anaemia	Number of Patients (%)		
	Baseline (n=100)	After 6 Months (n=100)	After 12 Months (n=97)
No Anaemia			
Males (Hb >13 gm %)	4 (4.0)	6 (6.0)	10 (10.31)
Females (Hb >12 gm %)	3 (3.0)	7 (7.0)	16 (16.49)
Mild			
Males (Hb 10-13 gm %)	26 (26.0)	28 (28.0)	34 (35.05)
Females (Hb 10-12 gm %)	15 (15.0)	19 (19.0)	18 (18.56)
Moderate (Hb 7.0-9.9 gm %)	46 (46.0)	28 (28.0)	10 (10.31)
Severe (Hb <7.0 gm %)	6 (6.0)	1 (1.0)	0 (0.00)
Chi Square	49.31		
p Value	<0.0001		

Table 4. Haematological Abnormalities in HIV Infected Patients

Other haematological abnormalities detected were leucopenia in 2% of cases, neutropenia in 3% of cases, lymphocytopenia in 18% of cases and thrombocytopenia in 9% of cases at the time of presentation. RBC count was less than lower limit of normal in 28% of females and 49% of males at the time of presentation. Lymphocytopenia was reduced to 12% of cases after 6 months of therapy which further reduced to 7.22% of cases after 12 months of therapy. No case of neutropenia was detected after 6 months of therapy and 1 case was detected as neutropenia after 12 months of therapy. Three cases showed thrombocytopenia after 6 months of therapy six cases after 12 months of therapy (Table-5).

Haematological Abnormalities	Number of Patients (%)		
	Baseline (n=100)	After 6 Months (n=100)	After 12 Months (n=97)
Neutropenia	3 (3.0)	0 (0.0)	1 (1.03)
Leucopenia	2 (2.0)	1 (1.0)	0 (0.0)
Lymphocytopenia	18 (18.0)	12 (12.0)	7 (7.22)
RBC Count (m/mm^3) (<3.8-Females)	28 (28.0)	16 (16.0)	14 (14.43)
RBC Count (m/mm^3) (<4.5-Males)	49 (49.0)	39 (39.0)	36 (37.11)
Thrombocytopenia	9 (9.0)	3 (3.0)	6 (6.19)

Table 5. Haematological Abnormalities in HIV Infected Patients at Different Time Periods

Table 6 shows mean CD4 count which at baseline was 280.44 ± 152.24, after 6 months of follow up was 351.77 ± 161.69 and after 12 months, there was a statistically significant increase in mean to 397.37 ± 167.95 with p value of <0.0001.

Haematological Parameter	Mean ± Standard Deviation			p Value
	Baseline (n=100)	After 6 Months (n=100)	After 12 Months (n=97)	
CD4 Count (cells/µl)	280.44 ± 152.24	351.77 ± 161.69	397.37 ± 167.95	<0.0001

Table 6. CD4 Count in HIV Infected Patients at Different Time Periods

DISCUSSION

In present study, the result of data analysis obtained shows a predominance of males amongst 100 patients that is males constituted 58% (n=58) with male: female ratio of 1.38:1. Similar sex distribution results were obtained in studies of Mitra JK et al.,[8] (2015) with a male to female sex ratio of 1.12:1 and Devi CS et al.,[9] 2016 with a male to female sex ratio of 1.9:1.

The patient age in the present study was from more than 16 years and 71% of the patients were in the age group of 21 to 40 years with mean age of 36.59 ± 9.12, which as per the fact is the sexually active part of life as well as highly productive age group. This is comparable with the findings of Mitra JK et al.,[8] (2015) where majority of the patients 21 to 40 years. This is also consistent with the findings of Devi CS et al.,[9] (2016), mean age of 39.8 ± 10.7. Parinitha SS and Kulkarni MH[10] showed similar results with mean age of 34.55 ± 9.63. In the present study compared to male age distribution, females were younger, 35.71% of them were between 21 to 30 years of age group.

Hematologic changes have been accepted as powerful determining predictors of morbidity and mortality in HIV-infected patients (Doukas MA, 1992).[11] It has been demonstrated that severe anaemia is linked with faster rate of HIV disease progression (Mocroft A et al., 1999).[12] Haematological abnormalities commonly encountered in HIV- infected individuals are anaemia, granulocyte disorders, thrombocytopenia, lymphomas, coagulopathies and vascular malignancies like Kaposi sarcoma. Although in majority of cases, haematological abnormalities are detected in middle or advanced stages of HIV infection, some of these like anaemia and thrombocytopenia have been reported to occur in early stages of HIV infection (Basu A et al., 1999).[13]

Anaemia is the most common cytopenia in HIV-infected individuals, occurring in 10-20% of patients at initial presentation and diagnosed in approximately 70 -80% of patients over the course of disease. The incidence is strongly related with the progression of the disease and is common in the symptomatic group (Spira TJ et al.,[14] 1993; Laurence J et al.,1996;[15] Sloand E, 2005;[16] Kasthuri AS et al.,[2] 2006; Mehta PS, 2007;[17] Wanchu A et al., 2009).[18]

In our study anaemia was present in 93% of cases. A similar observation was made by Kaloutsi et al.,[19] (1994) in 34/40 (85%) cases. Karcher et al.,[20] (1991) reported anaemia in 175/197 (89%) patients, and Tripathi et al.,[21] (2005) in 61/74 (82.4%) patients. However, Sitalakshmi et al.,[22] (2003) reported anaemia in 27/42 (64.2%) cases which is much lower as compared to the present study. Of these, severe anaemia was observed in 6% of cases as compared to 7% (Wanchu A et al., 2009),[18] 18.5% (Meidani A et al., 2012),[23] 33% (Kasthuri AS et al., 2006)[2] in various studies. 46% patients were moderately anaemic, 41% patients had mild anaemia and 7% patients had no anaemia. Overall frequency of anaemia in our study was comparable with other studies 9% cases had thrombocytopenia which in agreement with the study carried by Patwardhan et al.,[24] (2002) who had found thrombocytopenia in 13% of the cases. Sullivan et al.,[25] (1997) reported one year incidence of thrombocytopenia in 8.7% persons with one or more AIDS defining illness. We also observed leucopenia in 2% patients and neutropenia in 3% of cases. Neutropenia tend to occur concomitantly with anaemia, 10 to 30% of those with ARC may be neutropenic, this may progress to about three-quarters of those with AIDS (Zon et al., 1987).[26] Lymphopenia was seen in 18% of the cases. Similar observations was made by Tripathi et al.,[21] (2005) in 25.6% cases. All of these patients were followed after 6 months and 12 months of therapy and various haematological parameters were evaluated at these intervals. It is found that RBC parameters- haemoglobin, RBC count, haematocrit and MCHC showed statically significant improvement after 6 months and 12 months of therapy. MCV and MCH also showed improvement after 6 months and 12 months of therapy although it was not statically significant. This difference is probably due to improvement in these parameters after the initiation of HAART. Thulasi RR et al.,[27] (2016) also found the incidence and severity of anaemia slightly higher among the patients not receiving anti-retroviral therapy. Statically significant improvement was seen in platelet count after 6 months and 12 months of therapy. Other haematological parameters like total leukocyte count, absolute neutrophil count and absolute lymphocyte count did not show any significant improvement after 6 months and 12 months of therapy, the reason being toxicity of therapies for HIV or associated conditions. An autoimmune mechanism involving antigranulocyte antibodies and impaired granulopoiesis and any infiltrative process involving the bone marrow (infection, malignancy) has also been postulated (Donald W et al.,1998).

CONCLUSION

- This study shows that there was improvement in all parameters in these patients and also in the stage of disease when they were followed for one year after the initiation of HAART.
- So regular follow up and compliance of patient is of utmost importance in checking the progress of disease as well as ensuring better quality of life.
- Hence early diagnosis, appropriate treatment, haematinics and nutritious diet are the key factors for longer survival and good quality of life.
- At the same time, campaign for health education and preventive measures should be a continuous process so

that the affected individual will come forward to these designated centers and avail the facilities.

- Heath workers, social organisations and civil society should be educated so that they are aware of this permanent infection and take appropriate measures at all levels and this will help to overcome the social stigma attached to it.

REFERENCES

[1] WHO global program on AIDS. Current and future dimensions of HIV/AIDS pandemic a capsule summary. Geneva: WHO April 1991.

[2] Kasthuri AS, Sharma S, Kar PK. A study of "haematological manifestation of HIV infection at HIV tertiary care" center over a period time March 1998 to August 1999. Majority was inpatient and a few outpatients Bangalore. Sample size (n=100) HIV infected patient. Indian Journal Sex Transmission Disease 2006;27:1-9.

[3] Dhurve SA, Dhurve AS. Comparison of peripheral smear findings with bone marrow findings in HIV patients. Sch J Med Sci 2014;2(2C):711-717.

[4] Amegor OF, Bigila DA, Oyesola OA, et al. Haematological changes in HIV patients placed on anti-retroviral therapy in Markurdi, Benue state of Nigeria. Asian J of Epidemiol 2009;2(4):97-103.

[5] Dai Y, Qiu ZF, Li TS, et al. Clinical outcomes and immune reconstitution in 103 advanced AIDS patients undergoing 12-month highly active antiretroviral therapy. Chinese Med J (Engl) 2006;119(20):1677-1682.

[6] Owiredu WK, Quaye L, Amidu N, et al. Prevalence of anaemia and immunological markers among Ghanaian HAART naïve-HIV patients and those on HAART. Afr Health Sci 2011;11(1):2-15.

[7] Huruy K, Mulu A, Mengistu G, et al. Immune reconstitution inflammatory syndrome among HIV/ AIDS patients during Highly active antiretroviral therapy in Addis Ababa, Ethiopia. Japan J Infect Dis 2008;61(3):205-209.

[8] Mitra JK, Horo SM. Analysis of haematological profile in HIV positive patients before and after antiretroviral therapy. Int J Health Sci Res 2015;5(11):18-24.

[9] Devi CS, Satish S, Gupta M. A study of haematological profile in human immune deficiency virus infection: correlation with CD4 counts. Ann Pathol Lab Med 2016;3(5):484-489.

[10] Parinitha S, Kulkarni M. Haematological changes in HIV infection with correlation to CD4 cell count. Australas Med J 2012;5(3):157-162.

[11] Doukas MA. Human immunodeficiency virus associated anemia. Med Clin North Am 1992;76(3):699-709.

[12] Mocroft A, Kirk O, Barton SE, et al. Anaemia is an independent predictive marker for clinical prognosis in HIV-infected patients from across Europe. EuroSIDA study group. AIDS 1999;13(8):943-950.

[13] Basu A, Ghosh K, Banerjee K. Bone marrow involvement in HIV infection: light, electron and immune-electron microscopic studies. Indian J Hematol Blood Transf 1999;17(4):76-86.

[14] Spira TJ, Jones BM, Nicholson JK, et al. Idiopathic CD4+ T-lymphocytopenia--an analysis of five patients with unexplained opportunistic infections. N Engl J Med 1993;328(6):386-392.

[15] Laurence J, Mitra D, Steiner M, et al. Apoptotic depletion of CD4+ T cells in idiopathic CD4+ T lymphocytopenia. J Clin Invest 1996;97(3):672-680.

[16] Sloand E. Hematologic complications of HIV infection. AIDS Rev 2005;7(4):187-196.

[17] Mehta PS. Hematologic manifestations in HIV/ AIDS. In: HIV curriculum. 4th edn. Baylor College of Medicine 2007:222-228.

[18] Dikshit B, Wanchu A, Sachdeva RK, et al. Profile of heamatological abnormality of Indian HIV infected individual. BMC Blood Disorders 2009;9:5.

[19] Kaloutsi V, Kohlmeyer U, Maschek H, et al. Comparison of bone marrow and hematologic findings in patients with human immunodeficiency virus infection and those with myelodysplastic syndromes and infectious diseases. Am J Clin Pathol 1994;101(2):123-129.

[20] Karcher DS, Frost AR. Bone marrow in human immunodeficiency virus (HIV)-related disease morphology and clinical correlation. Am J Clin Pathol 1991;95(1):63-71.

[21] Tripathi AK, Karla P, Kumar A, et al. Study of bone marrow abnormalities in HIV disease. J Assoc Physicians India 2005;53:105-110.

[22] Sitalakshmi S, Srikrishna A, Damoder P. Haematological changes in HIV infection. Indian J Pathol Microbiol 2003;46(2):180-183.

[23] Meidani M, Rezaei F, Maracy MR, et al. Prevalence, severity and related factors of anemia in HIV/AIDS patients. J Res Med Sci 2012;17(2):138-142.

[24] Patwardhan MS, Golwilkar AS, Abhyankar JR, et al. Haematological profile of HIV positive patients. Indian J Pathol Microbiol 2002;45(2):147-150.

[25] Sullivan PS, Hanson DL, Chu SY, et al. Surveillence for thrombocytopenia in persons infected with HIV: results from the multistate adult and adolescent spectrum of disease project. J Acquir Immune Defic Syndr Hum Retrovirol 1997;14(4):374-379.

[26] Zon LI, Arkin C, Groopman JE. Haematologic manifestations of the human immune deficiency virus (HIV). Br J Hematol 1987;66(2):251-256.

[27] Thulasi RR, Manimaran D, Hemanathan G, et al. Haematological abnormalities in HIV infected individuals in correlation to CD4 counts and ART status. Asian J of Med Sciences 2016;7(4):14-18.