Original Research Article

Analysis of Hematological Profile in HIV Positive Patients before and After Antiretroviral Therapy

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ABSTRACT

Introduction: The treatment of HIV infection with highly active antiretroviral therapy (HAART) has been accepted as the gold standard in the management of HIV patients. The people living with HIV AIDS (PLWHA) have various types of hematological disorders of various degrees of varying severity at presentation.

Materials & Methods: A prospective cohort study was conducted to assess the hematological profile of HIV infected individuals after initiation of HAART at Rajendra Institute of Medical Sciences during the period of January 2012 to September 2013.A NACO standardized data extraction format was used to record the sociodemographic characteristics, clinical information and hematological parameters of the study subjects. All covariates for each patient were collected at 0,6 and 12 month following initiation of HAART.

Result: A total of 100 patients were studied, 53 (53%) were males as against 47 (47%) females with a sex ratio of 1.12:1.The haematological profile were presented as mean±SD as appropriate. Percentages were used to describe the proportions of the discrete variables. A p value <0.05 was considered statistically significant.

Conclusion: There was a significant improvement in CD4 cells and hemoglobin was observed after 6 months of HAART. Improvement in total count, absolute neutrophil count, absolute lymphocyte count was observed after 12 months of HAART. It can be concluded that in people living with HIV/AIDS, HAART is useful for modifying the mortality and morbidity.

Keywords: HIV, AIDS, haematology, CD4.

INTRODUCTION

Human Immunodeficiency virus (HIV) is the causative agent of Acquired Immunodeficiency syndrome (AIDS). Due to large scale of morbidity and mortality it causes, HIV is fast becoming Major threat in developing/third world countries. [1]

Every day, more than 6800 people become infected with HIV and more than 5700 die pr day, mostly because they have no access to HIV prevention, treatment and care services. Despite progress made in scaling up the response over the last decade, the HIV pandemic remains the most serious infectious disease challenge to global public health. [2]

HIV is characterized by progressive damage to the body's immune system which results in the development of a number of opportunistic infections and other complications. The haematologic complications of HIV infected patients include anaemia, neutropenia, lymphopenia and thrombocytopenia.

Anemia is the most commonly encountered haematologic abnormalities in HIV patients, occurring with increasing frequency and is a significant predictor of progression to AIDS or death, with more than 70% of patients developing anaemia and requiring transfusion (Omoregie R et al, 2009). [3]

According to Murphy MF et al, the incidence of lymphopenia, neutropenia and thrombocytopenia in patients with AIDS was 75%, 20% and 30% respectively and in patients with asymptomatic HIV positive patients the incidence was 15%, 0% and 0% respectively (Rombauts B, 1997). [4]

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). Combination of several, typically three or four drugs are known as Highly active Retroviral therapy (HAART). Combination of drugs create multiple obstacles to HIV replication to keep the number low and reduce the possibility of a superior mutation arising. These drugs must be taken in combination in order to have lasting effect. [5] Immune reconstitution in AIDS patients after HAART has been reported in several countries. [6-8]

Most studies have described the hematological parameters of HIV infected individuals after receiving HAART, however to our best knowledge there is only few published report in India that assessed the hematological parameters after receiving HAART.

Hence the aim of the present study is to assess hematological profile among HIV infected adult individuals after initiation of HAART and to compare the mean differences of selected haematological profile between baseline, after 6 months and 12 months after initiation of HAART.

MATERIALS AND METHODS
Study design: A prospective study was conducted to assess hematological profile among HIV infected individuals after initiation of HAART at ART clinic of Rajendra Institute of Medical Sciences (RIMS), Ranchi. Prior to the start of the study a pilot study was conducted to determine the prevalence of HIV infected patients.

Study population: Ethical clearance was obtained The study participants were HIV infected individuals who had started HAART by WHO criteria attending to the Department of Medicine/ART centre, RIMS during the period of January 2012 to September 2013 were taken up for the study. A total of 100 patients participated in the study.

Inclusion criteria: Participants with age group above 20 yrs were included. Baseline (preHAART) and six and twelve months follow up data with complete hematological values (TLC, CD4+ T cells, Hb, Neutrophils and lymphocytes)

Exclusion criteria: Patients with previously known hematological disorders, any congenital hematological disorders and age group less than 20 were excluded.

Demographic and Clinical data: Participants demographic variables, prophylaxis taken and type of ART regimen, hematological (Total leucocyte count, CD4+ T cells, hemoglobin, Neutrophils and lymphocytes) values were carefully extracted from ART log book and patient follow up cards by using standardized data extraction form which was prepared from ART log book.

Measurement and Data collection: A NACO standardized data extraction format was used to extract socio demographic characteristics, clinical information and hematological parameters of the study subjects from RIMS, Ranchi ART log book. All covariates for each patient were collected at 0 month, 6 month and 12 month following HAART initiation.

Hematological Abnormalities: Anemia defined as hemoglobin <13 gm/dl for men and < 12 gm/dl for women. Leucopenia defined as TLC count less than 3000 cells/µl. Neutropenia defined as absolute neutrophil count (ABLN) less than 1700 cells/ cumm. Lymphopenia 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 10-13gm/dl for men, moderate anemia is hemoglobin values of 8-9.9 gm/dl and severe anemia defined as hemoglobin values less than 8gm/dl. Immunosuppression defined as a CD4+T cell count < 200 cells/ µl.

Statistical analysis: The data collected through a standardized questionnaire were entered into excel spread sheet and transported into and analysed by Medcalc version 11.2.1.0. Values were presented as mean±SD .Percentages were used to describe the proportions of the discrete variables. A p- value <0.05 was considered statistically significant.

RESULT

In the present study a total of 100 patients were studied, 53 (53%) were males as against 47 (47%) females with a sex ratio of 1.12: 1.These 100 patients were studied and the clinical and hematological parameters were analyzed. Most of the patients in male were in the age group of 31-40 (22%) and females were in age group of 21- 30 (26%).In the study group the cases were selected from different age groups. In age group > 60 years males were 1 (1%) and females were nil. (Fig. 1)
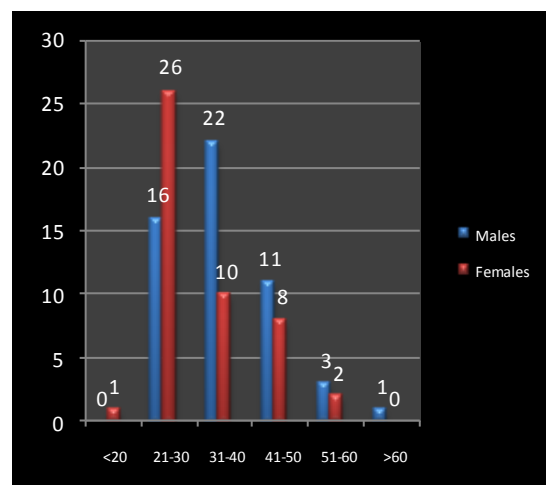

Fig 1: Distribution of the HIV positive patients according to age and sex

Table 1. Hematological parameters in HIV infected males and females

Haematological parameters	Baseline (n=100) mean±SD	After 6 months mean±SD	p value	After 12 months mean±SD	p value
Hb%	10.33±1.63	10.43±1.61	0.663(NS)	11.07±1.66	0.001(S)
TLC (cell/cumm)	6353.20±2339.94	6681.50±1597.40	0.247(NS)	7182.25±2192.94	0.010(NS)
ABNC(cell/cumm)	3620.78±1640.23	3651.19±1241.37	0.882(NS)	4148.75±1966.62	0.04(S)
ABLC(cell/cumm)	2145.89±952.93	2029.89±618.09	0.308(NS)	2468.72±985.42	0.019(NS)
CD4 count (cell/cumm)	263.27±165.17	287.37±134.14	0.258(NS)	331.40±140.99	0.002(S)

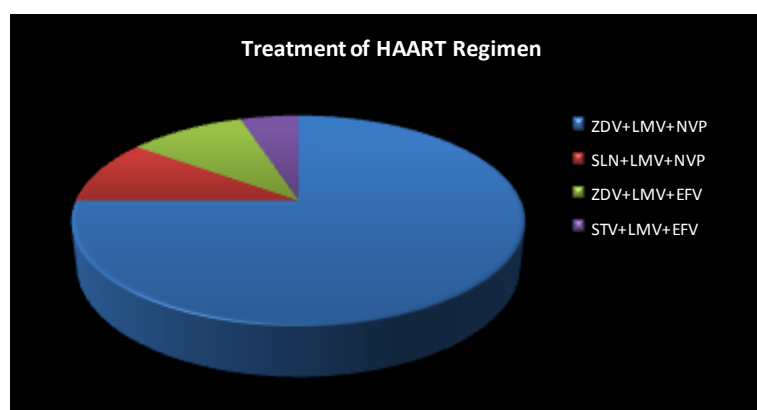NS- statistically Non significant; S- statistically significant

Fig 2: Treatment of HAART Regimen used in the study

Table 2: Haematological abnormalities

Haematological abnormalities	Baseline (n=100)		After 6months (n=100)		After 12 months (n=100)	
	Number	%	Number	%	Number	%
Leukopenia (WBC <3000/mm^3)	10	10	3	3	1	1
Neutropenia(<1700/mm^3)	14	14	5	5	1	1
Lymphopenia(<1500/mm^3)	20	20	13	13	15	15
Anaemia Mild:						
Male (10-13 gm%)	40	40	33	33	41	41
Female(10-12 gm%)	18	18	26	26	32	32
Moderate: (8-9.9 gm%)	28	28	27	27	14	14
Severe (<8gm%)	8	8	6	6	3	3
CD4 + T count <200 cell/µl	47	47	30	30	20	20
CD4+T count <50 cell/µl	2	2	0	0	0	0

Table 1 shows the mean hemoglobin at baseline(prior to HAART) is 10.33±1.63which after 6 months of HAART is 10.43±1.61(p= 0.663) and after 12 months there was a statistically highly significant increase in mean to 11.07± 1.66.The graph shows that there was statistically no significant difference between the hematological parameters at baseline to 6 months but a statistically highly significant increase in CD4 count was observed after 12 months (p=0.002) and statistically significant increase in TLC (p=0.010), ABNC (p=0.04),and ABLC(p=0.019) after 12 months.

Figure 2 shows that out of 100 cases, Zidovudine ZDV+ LMV+ NVP combination was used in 75% of cases followed by SLN+ LMV+ NVP and ZDV+ LMV+ EFV 10% of each. STV+ LMV+ EFV was used in 5% cases. (ZDV-Zidovudine, LMV- Lamivudine, NVP-Nevirapine, EFV- Efavirenz, STV-Stavudine)

Table 2 Out of the 100 cases leucopenia was observed in 10% cases while the rest had TLC within the normal range. After 6 months of HAART 7% improved while the rest 3% did not show improvement which after 12 months increased to 9% improvement. Neutropenia was seen in 14% of the total cases which after 12 months of HAART regimen only 2% showed improvement. Lymphopenia was present in 20% of the cases, of which after 12 months 5 % showed improvement. The comparison of haemoglobin shows that there was improvement after 12 months of HAART regimen as severe anaemia was reduced from 8% to3% of cases. There was also improvement with CD4+T count.

DISCUSSION

The result of the data analysis obtained shows a predominance of males amongst 100 patients that is males constituted 53% (n=53). As reported by Manisha S. Patwardhan et al (2002) [9] the sex distribution is not in accordance.

The patient age in the present study is from more than 20 years with 74% of patients in the age group of 21 to 40 years, which as per the fact is the sexually active part of life as well as highly productive age group. In the present study compared to male age distribution, females were younger, 55.32% of them were between 21 to 30 years of age group. There was no statistical significance to particular sex (p > 0.05).

Hematological parameters (white blood cell count, absolute neutrophil count, absolute lymphocyte count and CD4 + T cell count did not showed statistical significant change among males and females except mean haemoglobin (p<0.009) at the initiation of HAART.

Haematological parameters did not showed statistical significant change after six month of HAART initiation. Of 100 HIV infected adult individuals during the initiation of antiretroviral therapy revealed that the mean haemoglobin, white blood cell count, absolute neutrophil count absolute lymphocyte count and CD4+T

cell count were 10.43/dl IQR (6.8-14.4)gm/dl, 6681.5 cells/cumm IQR (2300-11250) cells/cumm, 3651.19 cells/cumm IQR (306-7844) cells/cumm, 2029.89 cells/cumm IQR (700-4275) cells/cumm and 287.37 cells/ cumm IQR (66-644) cells/cumm respectively.

Multiple haematological abnormalities including peripheral cytopenias usually observed in individuals infected with HIV (Bellari E, 1991). [9] Out of 100 patients, 47% (n=47) cases were those with CD4+T cell counts <200 cells/cumm and CD4+T cell count of < 50 cells/cumm was seen in 2% (n=2) of the patients, indicating the stage of severe immunosuppression. In contrast, with this other study conducted in India showed that 89.2% cases at baseline were with CD4 count < 200 cells/cumm and CD4+ T cell count of < 50 cells/cumm was seen in 18.6% of patients. [10]

In the present study, leucopenia was observed in 10% of patients before starting the treatment. This was lower compared to what has been reported from a study conducted in the university teaching hospital of Nigeria that described 16% leucopenia in people living with HIV/AIDS. [11]

HIV infection may lead to anemia in many ways; some of them are changes in cytokine production, decreased erythropoietin concentrations, opportunistic infectious agents. [12] The present study has shown that from the total 53 males; 52 (98.11%) and from the total of 47 females; 42 (89.36%) were anemic. The most occurred anemia in this study was mild anemia and this is also supported by study conducted in Iran described that mild anemia occurred in 46% of study subjects while severe anemia was not observed. [13] In agreement with our study another showed that from 155 HIV/AIDS patients at the baseline 35.5% were anemic. [8]

Our study showed that 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, at the baseline from the total of 100 patients 10(10%) were leucopenic and after 6 month HAART only 3(3%) were leucopenic. A retrospective study done at Zewditu memorial hospital Addis Ababa Ethiopia indicated that during initiation of HAART, the mean ± SD of WBC count of the total 1166 was 4767±1824 and after 6 months initiation of HAART increased to 6409±1998. [14]

Antiretroviral therapy decreases the prevalence of anemia in HIV infected patients and it is essential for the haemoglobin restoration of these patients. The present study compared hemoglobin values of 100 HIV infected patients at baseline and after 6 months initiation of HAART and 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 prevalence of anemia at the baseline was 89.36 % (42/47) and 98.1% (52/53) in females and males respectively. And after HAART only 93.61% (44/47) and 92.45% (49/53) in females and males respectively. This could be explained by that the regimen containing Zidovudine might be the cause which has led to fall in haemoglobin level. After 12 months it was 91.48 % (43/47) and 88.6% (47/53) for females and males respectively.

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).

A cross sectional study conducted in Rwandan women in Africa in the 2012 show that HIV +ve women have moderate neutropenia as compare to HIV-ve woman (4.2 Vs 0.5% ; p=0.006). In our study also the frequency of neutropenia is 14% before the start of HAART. [15]

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 were 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 at significant. HAART results in immunologic improvement, even among persons with low pretherapy CD4 + lymphocyte counts. Long term treatment with HAART restores the CD4 level of the patients, in our study patients data were observed for mean change of 12 months.

The significant improvement in CD4 cells and hemoglobin was observed after 6 months of HAART. The improvement in total count, absolute neutrophil count, absolute lymphocyte count were observed after twelve months of HAART which is consistent with the studies done at Addis Ababa University college of health science school of medicine. [8]

CONCLUSION

On the basis of above observation made in the prospective cohort study, the hematological disorders are very common in HIV patients. Anemia is a very important and common presentation in this group. HAART produces a definitive improvement of hematological parameters such as hemoglobin, absolute neutrophil count, absolute lymphocyte count, total count and CD4 count.

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How to cite this article: Mitra JK, Horo SM. Analysis of hematological profile in HIV positive patients before and after antiretroviral therapy. Int J Health Sci Res. 2015; 5(11):18-24.

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