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Research Article

PROFILE OF HEMATOLOGICAL ABNORMALITIES AND ITS CORRELATION WITH ABSOLUTE CD4 COUNT AND HIV VIRAL LOAD IN HIV-INFECTED PATIENTS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Objectives: The objectives of the study are as follows: (1) To study the spectrum of hematological abnormalities in human immunodeficiency virus (HIV) infected patients. (2) To find the correlation of hematological abnormalities with absolute CD4 count and HIV viral load.

Methods: This remained a cross-sectional and observational study conducted in the Department of General Medicine of Kamineni Academy of Medical Sciences and Research Centre, Hyderabad. The duration of the study was 18 months and it extended from January 2022 to June 2023. One hundred HIV-infected patients were included in this study on the basis of a predefined presence and exclusion criteria. CD4 count, complete blood count, CD4 count, and absolute neutrophil count were done in all cases. The spectrum of hematological abnormalities in HIV-infected patients and correlation of hematological abnormalities with absolute CD4 count and HIV viral load was analyzed. $p<0.05$ was taken as statistically important.

Results: Among the 100 studied cases, there were 62 (62%) males and 38 (38%) females with a M: F ratio of 1:0.61. The mean age of male and female patients was found to be 45.85±10.12 and 46.74±9.86 years. The mean age of male and female patients remained found to be comparable. Incidence of anemia and neutropenia was found to be more in patients with absolute CD4 count <200 cells/µl or viral load of >1000 copies/ml as compared to other patients and the difference was statistically significant ($p<0.05$). Although individuals with low absolute CD4 count (<200 cells/µl) or high viral load (>1000 copies/ml) had higher prevalence of thrombocytopenia there was no statistically significant difference from other patients ($p>0.05$).

Conclusion: Incidence of anemia and neutropenia significantly correlates with high HIV viral load and lower absolute CD4 cell counts.

Keywords: Human immunodeficiency virus, CD4 count, Viral load, Haematological abnormalities.

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INTRODUCTION

Hematological abnormalities represent a common clinical manifestation in persons infected with the human immunodeficiency virus (HIV). The interplay between HIV infection, immune system dysfunction, and hematopoietic alterations has been a subject of extensive research in the recent past [1]. HIV infection is characterized by its profound impact on the immune system, leading to a progressive depletion of CD4+ T lymphocytes, which play a pivotal role in the immune response against various infections. This immunological disruption not only renders individuals susceptible to opportunistic infections and malignancies but also influences the hematopoietic system. Hematological abnormalities frequently observed in HIV-infected patients encompass a wide spectrum, ranging from cytopenias such as anemia, neutropenia, and thrombocytopenia to dysregulated hematopoiesis and coagulopathy [2].

Anaemia is a hallmark of HIV infection and is multifactorial in origin. Chronic immune activation, cytokine dysregulation, nutritional deficiencies, and the direct impact of HIV on bone marrow function collectively contribute to the development of anemia. Neutropenia is often observed as a consequence of bone marrow suppression in the setting of advanced HIV disease [3]. Thrombocytopenia, attributed to both impaired platelet production and increased peripheral destruction, underscores the intricate interactions between the immune system and the hematopoietic system in the context of HIV infection. The CD4 count, a cardinal indicator of immune status, serves as a prognostic marker for HIV disease progression. As the HIV viral load rises, the CD4 count tends to decline, reflecting the extent of immune compromise. The correlation between hematological abnormalities and the absolute CD4 count is complex and bidirectional. Hematopoietic alterations can influence the immune milieu, and conversely, immune dysfunction can impact hematopoiesis. Understanding the interplay between these two facets is crucial for comprehensive patient management [4].

Equally significant is the role of the HIV viral load in shaping the hematological profile in HIV-infected patients. Elevated viral loads are associated with increased immune activation and inflammation, which can contribute to hematological disturbances. Furthermore, the direct impact of viral replication on bone marrow function and hematopoietic stem cells may exacerbate cytopenias and dysregulated hematopoiesis [5].

In recent years, the advent of antiretroviral therapy (ART) has transformed the management of HIV infection. ART not only suppresses viral replication but also allows immune reconstitution, leading to improvements in CD4 counts and a potential mitigation of hematological abnormalities. The intricate relationship between hematological parameters, viral load, and CD4 count in the era of ART underscores the need for continued investigation to optimize therapeutic strategies and improve patient outcomes [6]. Hematological abnormalities in HIV-infected individuals are reflective of the complex interplay between the immune system, viral replication, and bone marrow function. There is a need to provide a comprehensive analysis of the profile of hematological abnormalities in the context of HIV infection and their correlation with the absolute CD4 count and HIV viral load. Enhanced understanding of these relationships holds promise for refining prognostic assessments,

guiding therapeutic interventions, and advancing the overall management of HIV-infected patients [7].

This study aims to elucidate the profile of hematological abnormalities among HIV-infected patients and explore their correlation with two crucial indicators of disease progression: The absolute CD4 count and HIV viral load.

Aims and objectives

The objectives of the study are as follows:

1. To study the spectrum of hematological abnormalities in HIV-infected patients
2. To find the correlation of hematological abnormalities with absolute CD4 count and HIV viral load.

MATERIALS AND METHODS

This was a cross-sectional observational study conducted in the section of general medicine of Kamineni Academy of Medical sciences and Research Centre, Hyderabad. The duration of study was 18 months and it extended from January 2022 to June 2023. I00 patients infected with HIV were included in this study on the basis of a predefined addition and exclusion criteria. Keeping power (1-β error) at 80% and confidence interval (1-α error) at 95%, the minimum sample size required was 70 patients; therefore, we included 100 (more than minimum required number of cases) patients in this study. Institutional ethical committee approved the training and written informed consent was found from all the participants who expressed their willingness to be part of the study. Demographic details of all the patients such as age, gender, and socioeconomic status were noted.

Hematological profile that included hemoglobin level, red cell indices such as nasty corpuscular volume, mean corpuscular hemoglobin, and nasty corpuscular hemoglobin concentration, red cell distribution width, total leukocyte count, differential leukocyte count, platelet count, reticulocyte total, and peripheral smear examination was done in all cases. HIV viral load was determined by measuring polymerase chain reaction. In addition to above tests, CD4 count and absolute neutrophil count (ANC) were also done. The data were analyzed and a correlation between hemoglobin count versus absolute CD4 count, hemoglobin count versus HIV viral load, ANC versus absolute CD4 count, ANC versus HIV viral load, and platelet count versus absolute CD4 count was done.

Statistical analysis was done by SPSS version 21.0 software. Quantitative data were obtainable as mean and standard deviation. Qualitative data were presented with incidence and percentage tables. For quantitative data, unpaired t-test was applied and for qualitative data, Chi-square test was used. p value fewer than 0.05 was taken as statistically significant.

Inclusion criteria

The following criteria were included in the study:

- HIV-infected patients in whom HIV infection is confirmed by western blot or enzyme-linked immunosorbent assay.
- Age above 18 years.
- Patients who gave written informed consent to be part of study.
- Patients as both inpatient or outpatient.

Exclusion criteria

The following criteria were excluded from the study:

- Age <18 years.
- Pregnant patients.
- Patients who refused consent to be part of study.
- Patients in whom complete hematological profile was not available.
- Patients with hematological malignancies.
- Patients with pre-existing diseases likely to affect hemoglobin (Nutritional anemia, hemolytic anemia, and hemoglobinopathies), total leukocytes count (Lymphoma and leukemia), or platelet count (Idiopathic thrombocytopenic purpura, aplastic anemia, or hypersplenism).

RESULTS

Among the 100 studied cases, there were 62 (62%) males and 38 (38%) females with a M: F ratio of 1:0.61 (Fig. 1).

The most common affected age group was found to be above between 31 and 40 years (52%) followed by 41 and 50 years (32%). Six (6%) affected patients were above 50 years. Whereas 10 (10%) patients were below 30 years of age. The mean age of male and female patients was found to be 45.85±10.12 and 46.74±9.86 years. The mean age of male and female patients was found to be similar with no statistically significant difference (p=0) (Table 1).

HIV-infected patients having high viral load (>1000 copies/ml) and low CD4 count (<200 cells/mm^3) were found to have increased incidence of anemia. Out of nine patients having severe anemia, 7 (77.78%) were found to have absolute CD4 count of <200 cells/µl. The incidence of severe anemia was less in patients with absolute CD4 count of more than 500 cells/µl and only 1 (11.11%) patient with CD4 count of more than 500 cells/µl was found to be having severe anemia. The difference was found to be statistically significant (p<0.05). Similarly, out of eight patients having severe anemia 6 (75.00%) were found to have HIV viral load of >1000 copies/ml. The incidence of severe anemia was less in patients with HIV viral load of <200 copies/ml and only 1 (12.50%) patient with HIV viral load of <200 copies/ml was found to be having severe anemia. The difference was found to be statistically significant (p<0.05) (Table 2).

Studied cases having high viral load (>1000 copies/ml) and low CD4 count (<200 cells/mm^3) were found to have increased incidence of neutropenia. Out of 26 patients having ANC, <500/µl 21 (80.7%) were found to have absolute CD4 count of <200 cells/µl. The incidence of significant neutropenia was less in patients with absolute CD4 count of more than 500 cells/µl and only 2 (7.6%) patients with CD4 count of more than 500 cells/µl were found to have ANC <500/µl. The difference was found to be statistically significant (p<0.05). Similarly, out of 26 patients having ANC, <500/µl 19 (73.7%) were found to have HIV viral load of more than 1000 copies/ml. The incidence of significant neutropenia was less in patients with <200 copies/ml and only 3 (11.5%) patients with HIV viral load of more than 1000 copies/ml. The incidence of significant neutropenia was less in patients with <200 copies/ml that were found to have ANC

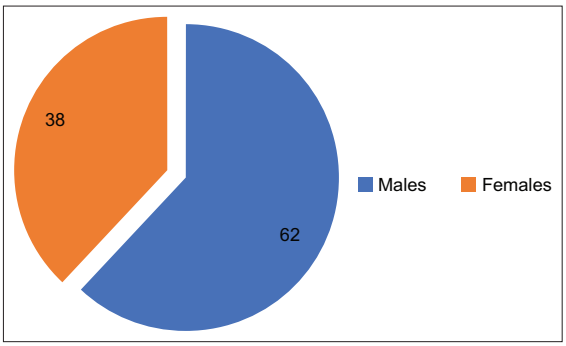

Fig. 1: Gender Distribution Of the studied cases

Table 1: Age distribution in the studied cases

Age in years	Males	Females
18–30 years	6 (6%)	4 (4%)
31–40 years	32 (32%)	20 (20%)
41–50 years	20 (20%)	12 (12%)
Above 50 years	4 (4%)	2 (2%)
Total	62 (62%)	38 (38%)
Mean age	39.52±14.36	37.62±13.96

p=0.517 (not significant)

<500/μl. The difference was found to be statistically significant (p<0.05) (Table 3).

Finally, the correlation of patients' platelet count and absolute CD4 count showed that though individuals with CD4 count < 200 cells/μl had higher prevalence of thrombocytopenia no statistically significant difference existed between absolute CD4 count and platelet count (P>0.05). Similarly, though individuals with high viral load >1000copies/ml had higher prevalence of thrombocytopenia, there was no statistically significant difference in the incidence of thrombocytopenia and HIV viral load as platelet count was found to be comparable in patients (p>0.05) (Table 4).

DISCUSSION

In our study of HIV-infected individuals, out of 100 cases, there were 62 (62%) males and 38 (38%) females with a M: F ratio of 1:0.61. The mean age of male and female patients stayed found to be comparable with no statistically significant difference (p>0.05). Visawale *et al*. conducted a prospective study to assess the HIV–TB coinfection in newly diagnosed HIV patients and correlate coinfection with CD4 and viral load (VL) [8]. In this study, out of total 94 HIV-TB coinfected patients, 59 (62.7%) were male and 35 (37.2%) were female. Male preponderance in this study was found to be similar to our study. However, many studies have found that women are more susceptible to get infected by HIV as compared to men. The reasons for this susceptibility of women to HIV infection as compared to men include economic dependence on their partners, lack of access to credible information on prevention of HIV infection, non-availability of diagnostic tests, and discrimination. Out of the abovementioned factors discrimination against women appears to be one of the important factors in developing world including India. Many infected women do not take anti-retroviral treatment and consequently may present with complications. Contrary to our study female preponderance was reported by the authors such as Magadi *et al.* [9] and Gheibi *et al*. [10].

In HIV-infected individuals a declining CD4 count signifies progressive immunosuppression, rendering individuals susceptible to opportunistic infections and malignancies. Concomitantly, diminished CD4 counts have been associated with heightened immune activation and inflammation, both of which can contribute to dysregulation of erythropoiesis and subsequent anemia [11]. On the other hand, viral load which is a reflection of viral burden within the host causes intensified immune system perturbation, characterized by heightened pro-inflammatory cytokine activity. This chronic inflammatory state has been implicated in the pathogenesis of anemia through various mechanisms, including direct suppression of erythropoiesis, impaired iron utilization, and increased destruction of red blood cells [12]. In our study, decreased absolute CD4 count and increased Viral load were found to be significantly associated with incidence as well as severity of anemia. Similar correlation between absolute CD4 count or increased viral load and incidence of anemia has also been reported by the authors such as Parinitha *et al.* [13] and Bhardwaj *et al*. [14].

Significantly reduced CD4 counts and indicative of immune dysfunction have been linked to heightened susceptibility to various infectious agents, including opportunistic pathogens that can precipitate neutropenia [15]. In addition, the profound impact of HIV on bone marrow function, often reflected in diminished CD4 counts, can lead to compromised granulopoiesis, contributing to neutropenia. Concurrently, viral load, indicative of viral replication dynamics, shapes the immune milieu in HIV patients. Elevated viral loads correspond to heightened immune activation and inflammation, processes intricately

Table 2: Correlation between absolute CD4 count, HIV viral load, and incidence of anemia

Haemoglobin level	Absolute CD4 count (%)			p value	HIV viral load (%)			p value
	>500 cells/μl	200–500 cells/μl	<200 cells/μl		<200 copies/ml	200–1000 copies/ml	>1000 copies/ml	
	N (%)	N (%)	N (%)		N (%)	N (%)	N (%)	
>12	18 (39.13%)	16 (34.78%)	12 (26.09%)	p<0.05 (significant)	36 (72.00%)	1 (2.00%)	13 (26.00%)	p<0.05 (significant)
10–12	07 (28.00%)	03 (12.00%)	15 (60.00%)		8 (36.36%)	1 (4.55%)	13 (59.09%)	
8–10	02 (10.00%)	01 (5.00%)	17 (85.00%)		2 (10.00%)	1 (5.00%)	17 (85.00%)	
<8	01 (11.11%)	01 (11.11%)	07 (77.78%)		1 (12.50%)	1 (12.50%)	6 (75.00%)	

Table 3: Correlation between absolute CD4 count, HIV viral load, and incidence of neutropenia

ANC	Absolute CD4 count (%)			p value	HIV viral load (%)			p value
	>500 cells/μl	200–500 cells/μl	<200 cells/μl		<200 copies/ml	200–1000 copies/ml	>1000 copies/ml	
	N (%)	N (%)	N (%)		N (%)	N (%)	N (%)	
1000–1500/μl	20 (38.4%)	15 (28.8%)	17 (32.6%)	p<0.05 (significant)	19 (36.5%)	14 (26.9%)	19 (36.5%)	p<0.05 (significant)
500–1000/μl	6 (27.2%)	4 (18.1%)	12 (54.5%)		6 (27.2%)	4 (18.1%)	12 (54.5%)	
<500/μl	2 (7.6%)	3 (11.5%)	21 (80.7%)		3 (11.5%)	4 (15.3%)	19 (73.7%)	

ANC=Absolute neutrophil count

Table 4: Correlation between absolute CD4 count, HIV viral load, and incidence of thrombocytopenia

Platelet count	Absolute CD4 count			p value	HIV viral load			p value
	>500 cells/μl	200–500 cells/μl	<200 cells/μl		<200 copies/ml	200–1000 copies/ml	>1000 copies/ml	
	N (%)	N (%)	N (%)		N (%)	N (%)	N (%)	
50,000–100,000/μl	24 (26.6%)	21 (23.3%)	45 (50.0%)	p>0.05 (not significant)	40 (48.7%)	3 (3.6%)	39 (47.5%)	p>0.05 (not significant)
20,000–50,000/μl	1 (50.0%)	1 (50.0%)	2 (50.0%)		3 (42.8%)	2 (28.5%)	2 (28.5%)	
<20,000/μl	1 (16.6%)	1 (16.6%)	4 (66.6%)		4 (36.3%)	1 (9.0%)	6 (54.5%)	

tied to bone marrow function and granulopoiesis [16]. Chronic immune stimulation, characteristic of higher viral loads, may lead to the production of immune mediators that disrupt the delicate balance of hematopoiesis, thereby contributing to neutropenia. Furthermore, direct viral interaction with hematopoietic progenitors can hamper neutrophil production, further exacerbating neutropenia. In our study, decreased absolute CD4 count and increased viral load were found to be significantly associated with incidence as well as severity of neutropenia. Similar correlation between absolute CD4 count or increased Viral load and incidence of neutropenia has also been reported by the authors such as Levine *et al.* [17] and Shi *et al.* [18].

Unlike hemoglobin levels and ANC in HIV patients, our study did not find a significant correlation between diminished CD4 count or increased viral load and risk of thrombocytopenia. Although diminished CD4 counts or increased viral load are known to be associated with altered megakaryocyte dynamics, potentially contributing to thrombocytopenia, we did not find any significant correlation between reduced CD4 count or increased viral load and risk of thrombocytopenia. In our study, though we found that individuals with low CD4 count before high viral load had higher prevalence of thrombocytopenia, there was no statistically significant difference. The authors such as Nascimento and Tanaka [19] and Marks *et al.* [20] have also reported increased incidence of thrombocytopenia in HIV-infected individuals.

CONCLUSION

It is important to assess HIV-infected individuals for the presence of hematological abnormalities so as to treat them effectively. In this study, incidence of anemia and neutropenia significantly correlated with high HIV viral load and lower complete CD4 cell counts. Furthermore, complete blood counts and peripheral smear have been suggested as the alternatives for the assessment of HIV-infected individuals since they significantly correlated with high HIV viral load and lower absolute CD4 cell counts.

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AUTHOR CONTRIBUTION

MB- Concept and design of the study, interpreted the results, prepared first draft of manuscript, and critical review of the manuscript; AV- Statistically analyzed and interpreted, reviewed the literature, and manuscript preparation; SB- Project of the study, statistically analyzed and interpreted, preparation of manuscript, and revision of the manuscript; SI and SM- Concept and coordination of the overall study.

CONFLICTS OF INTEREST

None.

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