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HEMATOLOGICAL ABNORMALITIES AND DISEASE PROGRESSION IN HIV-INFECTED PATIENTS: A PROSPECTIVE OBSERVATIONAL STUDY

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Abstract

Background: Acquired Immunodeficiency Syndrome (AIDS), caused by the Human Immunodeficiency Virus (HIV), results in gradual immune system deterioration and predisposes individuals to a variety of hematological abnormalities. These include anemia, leukopenia, neutropenia, thrombocytopenia, and other cytopenias, which are frequently associated with disease progression and CD4 counts. The purpose of this study was to look into the prevalence of hematological abnormalities in HIV-infected people and how they correlated with disease stages, CD4 levels, viral load, and patient outcomes.

Methods: A prospective observational study was carried out at Government Theni Medical College Hospital from October 2021 to September 2022. The study comprised 100 HIV-positive individuals who received a thorough hematological examination, including complete blood counts, CD4 cell counts, and viral load tests. The data were evaluated to determine the distribution of hematological abnormalities at various stages of HIV illness (Stages I-IV) and their relationship to clinical indicators. Statistical analysis was conducted using ANOVA for continuous variables and Chi-square testing for categorical variables, with significance set at $p < 0.05$.

Results: The study found a high prevalence of anemia, leucopenia, neutropenia, and thrombocytopenia in HIV patients, especially in the late stages of the disease. Anemia was most prevalent in Stage III, with significant gender differences ($p < 0.05$). Neutropenia and lymphocytopenia were also prevalent in Stage III, with thrombocytopenia following a similar trend. There was a strong association between low CD4 counts and the occurrence of these abnormalities. 86 percent of patients had a CD4 count < 200 cells/µL, indicating severe illness and immunosuppression.

Conclusion: Hematological abnormalities, including anemia, neutropenia, and thrombocytopenia, are frequent in HIV patients and worsen as the disease advances. These anomalies are closely related with low CD4 levels and advanced HIV infection. Monitoring hematological parameters can be an effective approach for monitoring disease progression and directing therapeutic interventions in HIV-positive people.

Keywords: HIV, AIDS, Hematological abnormalities, Anemia, Thrombocytopenia, WHO staging, Immunodeficiency

INTRODUCTION

Acquired Immunodeficiency Syndrome (AIDS) was initially detected in 1981, while Human Immunodeficiency Virus (HIV) was discovered in 1983 [1]. Globally, HIV/AIDS is best understood as a pandemic affecting almost every country [2]. In India, it was estimated that 2.27 million people had HIV/AIDS by the end of 2008, with an adult prevalence of 0.29% [3]. HIV infection causes the immune system to deteriorate gradually as the number of circulating CD4+ T-helper cells decreases. This predisposes HIV patients to a wide range of opportunistic infections and neoplastic diseases. AIDS is the most severe phase of HIV infection, characterized by a CD4+ cell count < 200 cells/mm³ and particular opportunistic infections [4]. HIV infection causes a multisystem illness with common hematological abnormalities. These hematological abnormalities worsen in the late stages of the disease, indicating the role of active virus replication and high levels of viremia in disease etiology [5, 6]. Common hematological disorders include hematopoiesis defects, cytopenias that impact numerous cell lineages, and coagulation abnormalities. These difficulties come from a variety of sources, including immune-mediated cell damage, direct cytopathic effects of the virus, secondary infections and neoplasms, and medication toxicity [7]. Anemia is the most common hematological condition seen in HIV-infected children and adults. Anemia is particularly common in patients with late-stage illness and low CD4 cell levels. Anemia has been connected to disease progression and an increase in mortality [8]. Anemia in HIV-infected patients is usually normocytic and normochromic, with a low reticulocyte count [9].

The causes of anemia are diverse, involving three primary mechanisms: (1) decreased red blood cell (RBC) production due to opportunistic infections, the direct effect of HIV, myelosuppressive medications, decreased production of erythropoietin, or hypogonadism; (2) increased RBC destruction, which can occur due to autoimmune hemolytic anemia, thrombotic microangiopathy, or disseminated intravascular coagulation; and (3) ineffective RBC production, often linked to folic a In impoverished countries, nutritional deficiencies, such as a lack of vitamins and iron, are frequent. The degree of inflammation and its impact on hemoglobin levels may be important indicators of illness severity and prognosis [10]. Leukopenia is very prevalent, especially in patients with severe illness. Neutropenia has been detected at all phases of the disease, but lymphopenia, which largely affects CD4 T-helper cells, is regarded as a traditional marker of HIV infection. Lymphopenia worsens as the disease progresses [11].

HIV-infected individuals frequently exhibit dysplastic neutrophil alterations, such as odd nuclei, high nuclear-to-cytoplasmic ratios, hypogranularity, and nuclear fragmentation [12]. Thrombocytopenia can develop at any stage of HIV infection, but it is most common in late-stage disease and in patients with low CD4 cell levels. Myelodysplastic alterations are typically seen in HIV patients and can be discovered at any stage of the disease. The most prevalent infectious agents affecting bone marrow in AIDS patients are Mycobacterium, Histoplasma, and Toxoplasma [13, 14]. This observational study sought to determine the frequency of hematological abnormalities in HIV patients, as well as the relationship between anemia, neutropenia, and thrombocytopenia and CD4 cell counts, viral load, and mortality.

MATERIALS AND METHODS

Study design

This prospective observational study was carried out at Government Theni Medical College Hospital from October 2021 to September 2022.

Study Population

Sample Size: 100 HIV-positive patients

Inclusion Criteria

- ✓ Age above 18 years
- ✓ Confirmed HIV infection (Western blot or ELISA)
- ✓ Both inpatients and outpatients.

Exclusion Criteria

- ➢ Patients refusing consent
- ➢ Incomplete investigations
- ➢ Other causes of anemia
- ➢ Patients on anti-tuberculous therapy
- ➢ Bleeding disorders, chronic kidney disease, chronic liver disease
- ➢ Alcoholic patients
- ➢ Pregnant patients
- ➢ Patients on steroids, iron, or vitamin therapy
- ➢ Patients unwilling to participate

Hematological Analysis:

WBC, RBC, and platelet counts were determined using a direct current detection method. Blood samples were run through an automatic analyzer, which recorded electrical resistance changes as blood cells flowed through an aperture. On stained peripheral smears, a differential leucocyte count was done using the Leishmann stain. The Westergren method was used to assess the erythrocyte sedimentation rate (ESR).

CD4 Lymphocyte Count:

Performed with the BD FACS Calibur flow cytometer. Cells were treated with monoclonal antibodies CD3, CD4, and CD45, which allowed laser technology to measure cell size and granularity.

Statistical Analysis

The data was analyzed using ANOVA for continuous variables and the Chi-square test for categorical variables, with p-values < 0.05.

RESULTS

In this study, 100 HIV positive individuals who were referred to the haematology laboratory section for a full haemogram and had their CD4 count checked were included. Each of these patients had their haematologic parameters and CD4 levels evaluated.

Distribution of age group among the patients

The study included 100 HIV-positive patients, with an average age of 40.6 ± 11.41 years. The age distribution found that the majority of patients (26%) were between the ages of 30 and 39, followed by those aged 50 to 59 (25%). 22% of patients were between the ages of 20 and 29, with 24% aged 40 to 49. A lesser proportion of patients (3%) were aged 60 to 69 years (Fig. 1).

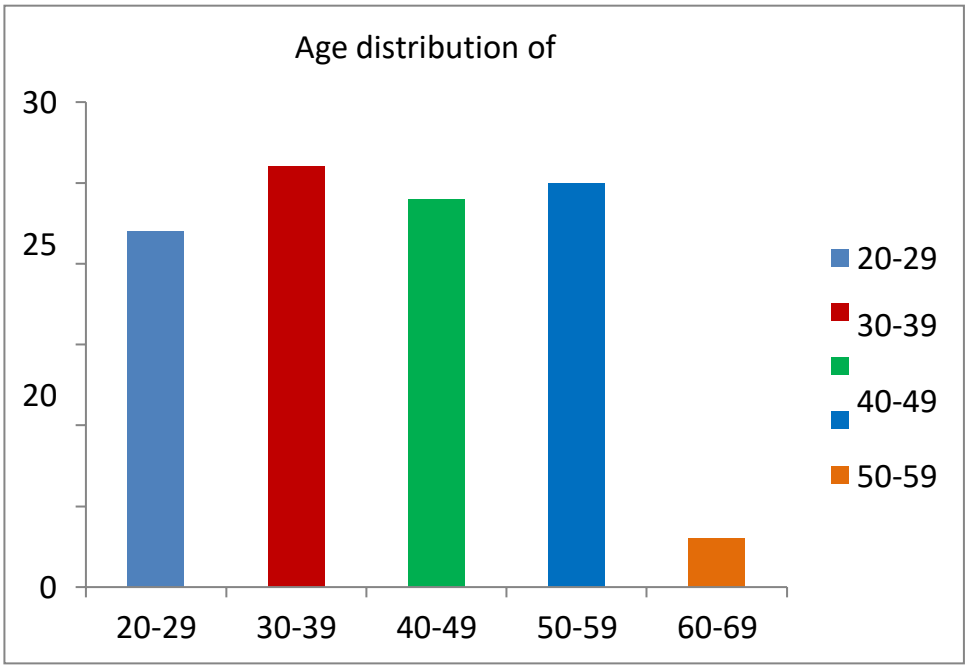

Fig 1: Graphical representation of age group among the patients

Distribution of gender

In terms of gender distribution, the study included 55 male patients (55%), and 45 female patients (45%). This implies a somewhat higher HIV infection rate among males in the research population. The gender distribution emphasizes the importance of gender-sensitive approaches in the management and care of HIV-positive people, as there may be disparities in illness presentation and response to therapy between men and women. Figure 2 displays the gender distribution calculated in this study.

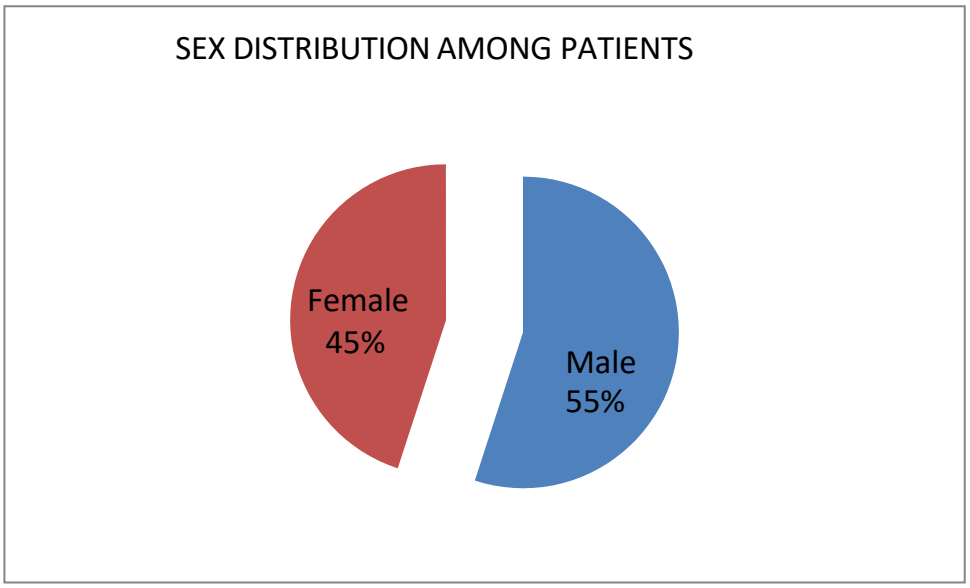

Fig 2: Graphical representation of gender distribution among the patients

Marital status of the patients

The results show the marital status distribution of the patients, with 87 married and 13 unmarried. This shows that the vast majority of patients are married, accounting for roughly 87% of the total, with unmarried patients accounting for approximately 13% (Fig.3).

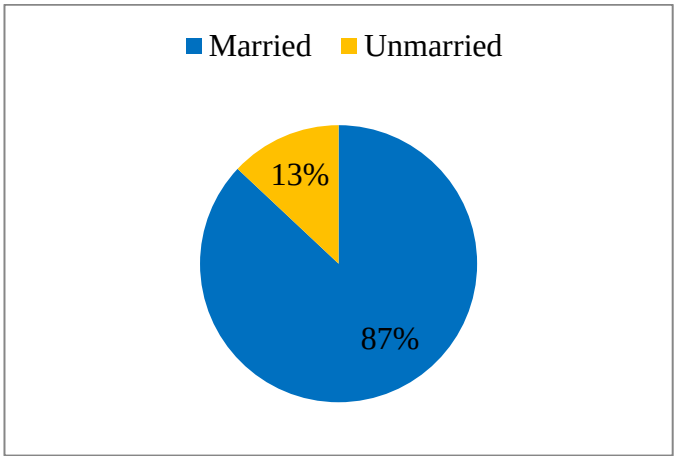

Fig 3: Graphical representation of marital status of the patients

Educational status of the patients

The data shows that 88 of the total patients are educated, whereas 12 are uneducated. This suggests that 88% of the patients have some level of education, while the remaining 12% are ignorant. The higher number of educated patients shows that the group has a higher level of education overall (Fig 4).

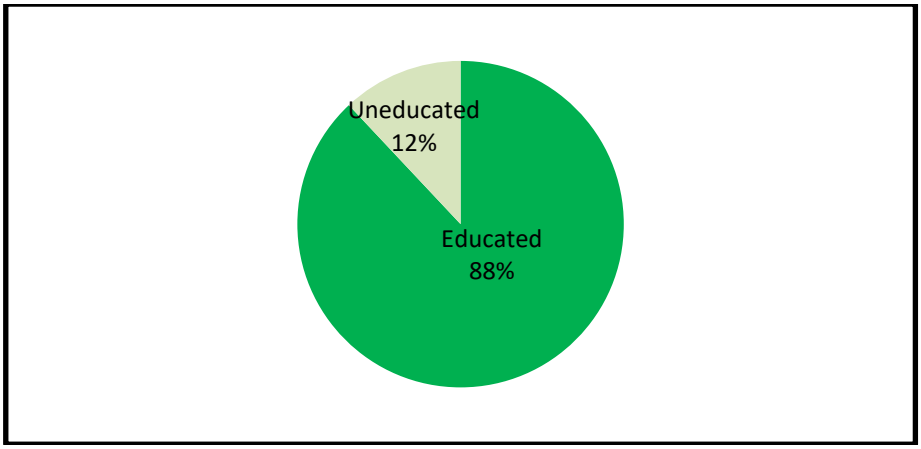

Figure 4: Graphical representation of educational status of the patients

Occupation of Patients

The results show that 70 patients are employed and 30 are unemployed. This means that 70% of the patients are employed and 30% are unemployed, indicating a higher number of employed people in this category (Fig.5).

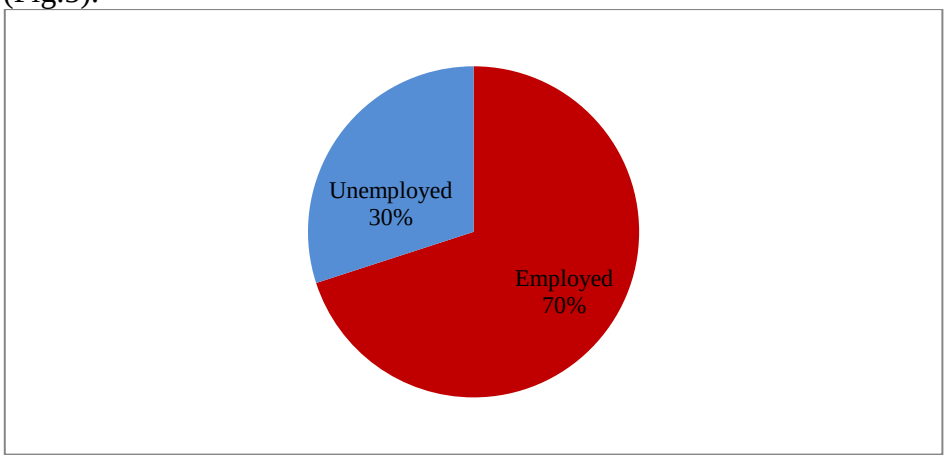

Figure 5: Graphical representation of occupation status of the patients

WHO Staging

This distribution demonstrates that the majority of patients are in Stage III (56 patients), accounting for 56% of the total. Stage II comprises 28 patients (28%), and Stage IV has 12 people (12%). Stage I is the smallest group, with only four people (4%). This shows that the majority of the patients in the study are in more advanced phases (III and II), with fewer in the early and severe stages (I and IV) (Fig.6).

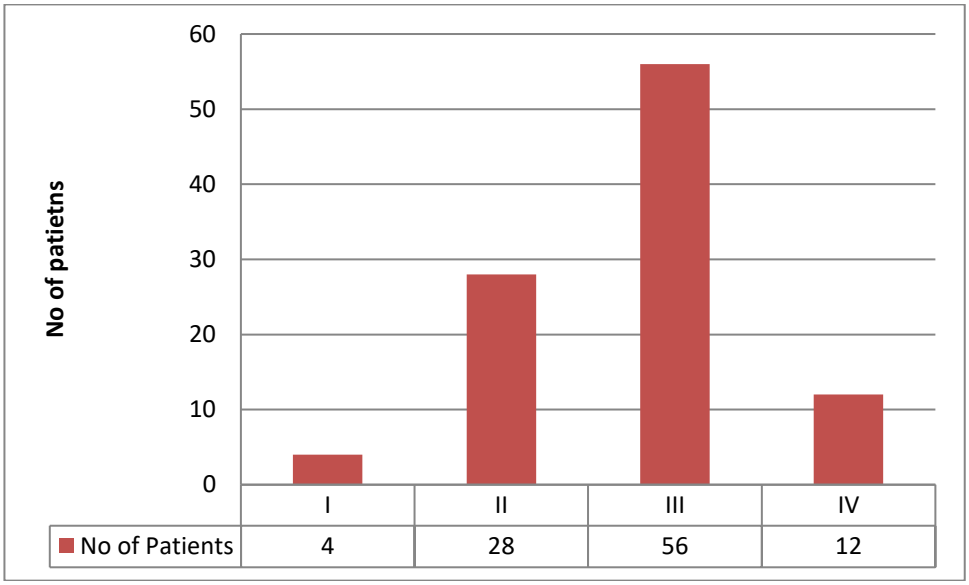

Figure 6: Graphical representation of WHO staging of patients

CD4 Count of Patients

The majority of patients (86%) had a CD4 count below 200 cells/µL, indicating a weakened immune system. Only one patient had a CD4 level higher than 500 cells/µL (Fig. 7).

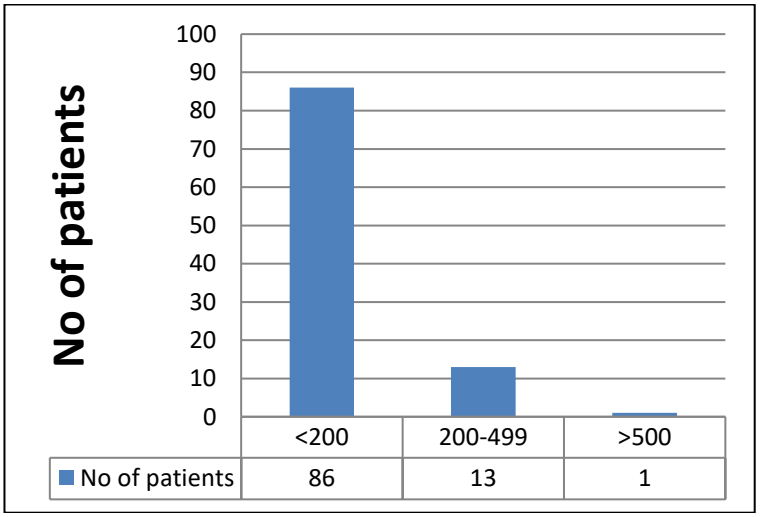

Figure 7 Graphical representation of CD4 Count of Patients

Total Count of Patients

This distribution shows that the majority of patients (22 patients, or 22%) fall within the 3001-4000 cells/mm³ range. The next largest group is in the 8001-9000 cells/mm³ range, with 18 patients (18%). Smaller groups are found in the 4001-5000 cells/mm³**,** 5001-6000 cells/mm³**,** and 7001-8000 cells/mm³ ranges. The smallest groups are in the 2000-3000 cells/mm³ and 9001-10000 cells/mm³ ranges, each with just 6–8 patients. This suggests a moderately distributed total cell count across different ranges, with a concentration in the mid-range of 3001-4000 cells/mm³ (Fig.8)**.**

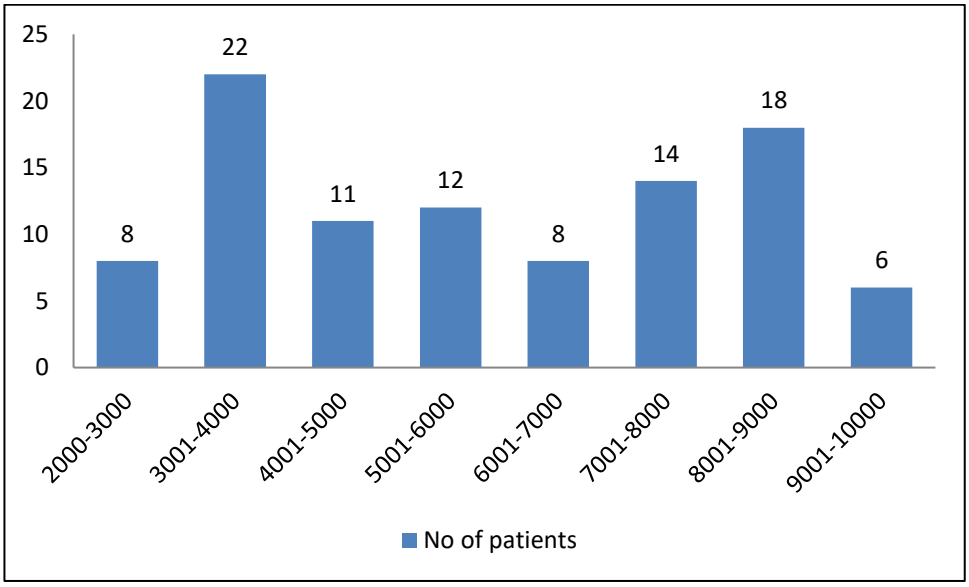

Figure 8: Graphical representation of total count of patients

Clinical and Laboratory Findings Across Patient Stages

The distribution of white blood cells (WBC) across cell types demonstrates that Neutrophils had the greatest mean value at 52.74 ± 12.45, showing they are the major cell type in the patients' blood, with some variance among people. Lymphocytes have a mean of 28.45 ± 8.24, indicating moderate presence of these immune cells. Monocytes and Eosinophils had low numbers, with mean values of 5.93 ± 3.6 and 2.54 ± 3.6, respectively, suggesting a lower function in the immunological response. Notably, Basophils were absent from this group, as evidenced by a count of zero.

The platelet count distribution among the patients is as follows: 24 patients fall within the 0.5-0.99 lakh/mm³ range, 19 patients are in the 1.00-1.49 lakh/mm³ range, and 29 patients have a platelet count in the 1.50-1.99 lakh/mm³ range, making it the largest group. There are 13 patients in the 2.00-2.49 lakh/mm³ range, 8 patients in the 2.50-2.99 lakh/mm³ range, and just 1 patient with a platelet count greater than 3.0 lakh/mm³. The data shows that 30 male patients and 25 female patients have elevated ESR (erythrocyte sedimentation rate) levels. This suggests a slightly higher prevalence of elevated ESR among males compared to females in the patient group. The elevated ESR indicates the presence of inflammation or other underlying conditions that could be affecting both male and female patients.

The hemoglobin levels for male and female patients show some distinct patterns. For both groups, the most common range is 10-12.9 gm/L, with a slight variation in the specific distribution between males and females. Males tend to have a wider spread across the ranges, with a notable number in the 11-11.9 gm/L and 12-12.9 gm/L ranges, while females are more concentrated in the 10-12.9 gm/L range, especially in the 12-12.9 gm/L category. Notably, no female patients fall in the 13-13.9 gm/L range, while 4 male patients do. Additionally, the **8**-8.9 gm/L range has a small number of males, but no female patients fall into this category, reflecting a slightly lower hemoglobin level in males compared to females in this group.

The distribution of various abnormalities across different stages (I, II, III, IV). Leucopenia is most common in Stage III, followed by Stage II, with smaller numbers in Stage I and IV. Neutropenia follows a similar pattern, with the highest occurrence in Stage III. Lymphocytopenia is also most frequent in Stage III, while Monocytopenia and Thrombocytopenia show a similar trend, with the highest numbers in Stage III, followed by Stage II. However, the p-values for all abnormalities are relatively high (ranging from 0.45 to 0.74), indicating that there is no statistically significant difference in the prevalence of these abnormalities across the stages. This suggests that the occurrence of these abnormalities is relatively consistent across different disease stages.

WHO Staging & Anemia

The statistics on anemia prevalence throughout multiple stages (I, II, III, and IV) show that both male and female patients have greater rates of anemia as the disease advances. Anemia is most common in male patients in Stage III (11 patients), followed by Stage II (6 patients), with fewer cases in Stage IV (4 patients), and none in Stage I. Female patients have the highest prevalence of anemia in Stage III (9 patients), followed by Stage II (7 patients), Stage IV (2 patients), and Stage I (0 patients). The p-values for both males (0.002) and females (0.0001) are statistically significant, indicating a robust link between illness progression and anemia in both genders. This suggests that anemia increases as the disease progresses, with substantial disparities between male and female individuals.

DISCUSSION

Anemia, neutropenia, thrombocytopenia, and lymphocytopenia are some of the most common hematological abnormalities seen in HIV-infected people. These anomalies are frequently suggestive of disease progression and immune system degradation, which are common hallmarks of HIV infection. In this study, we found that as HIV progressed, particularly in the advanced stages (III and IV), the prevalence and severity of these hematological disorders increased, suggesting the disease's immunosuppressive nature. Anemia was the most prevalent hematological abnormality in our cohort, with a significant increase in its prevalence as the disease advanced. This finding aligns with previous studies that have reported a high incidence of anemia in HIV patients, particularly in those with low CD4 counts [15]. The underlying causes of anemia in HIV patients are multifactorial, including decreased red blood cell (RBC) production, increased RBC destruction, and ineffective erythropoiesis due to chronic inflammation, opportunistic infections, or HIV-related bone marrow suppression [16]. The higher prevalence of anemia in Stage III (both in males and females) and its significant association with CD4 count ($p < 0.05$) highlight its potential role as an indicator of disease progression and immunosuppression. Neutropenia was also found primarily in advanced stages, notably Stage III, which is consistent with previous findings [17]. Neutropenia in HIV patients can be caused by the virus's direct cytotoxic effects on hematopoietic cells, immune-mediated damage, or the myelosuppressive effects of antiretroviral therapy. Dysplastic alterations in neutrophils, such as altered nuclear morphology, hypogranularity, and nuclear fragmentation, have been observed in HIV patients and may lead to poor immunological response [18]. Our study backs up previous findings, revealing a higher incidence of neutropenia in more advanced stages of HIV. Neutropenia was also identified largely in the latter phases, particularly Stage III, which is consistent with earlier research [19]. Neutropenia in HIV patients may be caused by the virus's direct cytotoxic effects on hematopoietic cells, immune-mediated damage, or the myelosuppressive effects of antiretroviral therapy. Dysplastic abnormalities in neutrophils, such as altered nuclear morphology, hypogranularity, and nuclear fragmentation, have been found in HIV patients and may contribute to a poor immune response [20]. Our work confirms earlier findings, indicating a higher incidence of neutropenia in more advanced stages of HIV. The CD4 count **i**s a well-established marker of HIV progression, and our findings reinforce the critical role of low CD4 counts in the development of hematological abnormalities. The majority of patients in our cohort had CD4 counts below 200 cells/μL, which is consistent with the findings of other studies that have shown a strong correlation between low CD4 levels and the occurrence of cytopenias, including anemia, neutropenia, and thrombocytopenia. This suggests that as the immune system weakens, the bone marrow function becomes increasingly compromised, leading to the development of these abnormalities. In this study Mean age group of the study was 40.6□11.41years and majority of patients belongs to 30-39 years of age. 55% of patients were males and 45% of patients were females. 87% were married and 12% were uneducated in this study group. The higher no. of patients was observed in stage III (No. of patients = 56). Similarly, very few patients was observed in stage I (No. of patients = 4). The majority of patients having <200 CD4 count was observed in this study; Santis et al. reviewed the Hematological abnormalities in HIV-infected patients and they found an association between CD4 count and hemoglobin level, neutrophil count, and platelet

count, and that anemia was independently associated with a higher mortality. In our study also we found association between hematological parameters and CD4 count [21]. Bhardwaj et al. conducted a cross sectional study on Hematologic derangements in HIV/AIDS patients and their relationship with the CD4 counts and found significant relationship was observed between the anemia, absolute lymphocyte count, and thrombocytopenia with the CD4 counts [22]. While the study provides valuable insights into the prevalence and patterns of hematological abnormalities in HIV patients, it is important to note that these abnormalities are not solely attributable to HIV infection. Other factors, such as coinfections, antiretroviral therapy, nutritional deficiencies, and comorbidities, can contribute to the development of cytopenias and affect the interpretation of hematological findings. Therefore, a comprehensive evaluation of each patient, considering their clinical history and other potential causes of hematological dysfunction, is crucial in managing HIV-associated hematological abnormalities effectively.

CONCLUSION

This study found that hematological abnormalities, including anemia, neutropenia, and thrombocytopenia, are common in HIV patients, particularly in advanced disease stages (III and IV). Anemia was most prevalent in Stage III and showed a significant association with lower CD4 counts. These findings underscore the importance of regular hematological monitoring in HIV patients, as these abnormalities can indicate disease progression and guide timely interventions. Early detection and management of hematological issues are crucial for improving patient outcomes in HIV care.

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Conflict of interest:
The authors report no conflicts of interest in this work.

REFERENCES

1. Loscalzo J, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL. Harrison's principles of internal medicine. (No Title). 2022 May.
2. Becerra JC, Bildstein LS, Gach JS. Recent insights into the HIV/AIDS pandemic. Microbial cell. 2016 Sep 9; 3(9):451.
3. Sehgal S. Unfolding of HIV Epidemic and Spectrum of AIDS in North India. World Journal of AIDS. 2014 Mar 4; 4(01):52-61.
4. Okoye AA, Picker LJ. CD 4+ T-cell depletion in HIV infection: mechanisms of immunological failure. Immunological reviews. 2013 Jul;254(1):54-64.
5. Dikshit B, Wanchu A, Sachdeva RK, Sharma A, Das R. Profile of hematological abnormalities of Indian HIV infected individuals. BMC hematology. 2009 Dec;9:1-6.
6. Kirchhoff F, Silvestri G. Is Nef the elusive cause of HIV-associated hematopoietic dysfunction?. The Journal of clinical investigation. 2008 May 1;118(5):1622-5.
7. Bhardwaj S, Almaeen A, Wani FA, Thirunavukkarasu A. Hematologic derangements in HIV/AIDS patients and their relationship with the CD4 counts: a cross-sectional study. International journal of clinical and experimental pathology. 2020;13(4):756.
8. Sullivan PS, Hanson DL, Chu SY, Jones JL, Ward JW, Disease Group TA. Epidemiology of anemia in human immunodeficiency virus (HIV)-infected persons: results from the multistate adult and adolescent spectrum of HIV disease surveillance project. Blood, The Journal of the American Society of Hematology. 1998 Jan 1; 91(1):301-8.
9. Olu-Taiwo A, Olatunya O, Amusu A, Akanmu A. Red Cell Characteristics in Anaemic HIV Infected Patients. British Journal of Medicine and Medical Research. 2016 Jan 10;15(8):1-7.
10. Antelman G, Spiegelman D, Narh R, Hunter DJ, Fawzi WW, Msamanga GI, Urassa EJ. Nutritional factors and infectious disease contribute to anemia among pregnant women with

human immunodeficiency virus in Tanzania. The Journal of nutrition. 2000 Aug 1;130(8):1950-7.
11. Evans RH, Scadden DT. Haematological aspects of HIV infection. Best Practice & Research Clinical Haematology. 2000 Jun 1;13(2):215-30.
12. Van Rhee JA. Hematologic System. Clin. Med. Phys. Assist. 2022 Feb 5;251(1).
13. Pasha I. A Study of Hematologic Manifestations in Patients with Hiv Infection (Doctoral dissertation, Rajiv Gandhi University of Health Sciences (India)).
14. Kaner JD, Thibaud S, Jasra S, Wang Y, Janakiram M, Sharma A, Sridharan A, Elias H, Polineni R, Assal A, Weiss L. HIV portends a poor prognosis in myelodysplastic syndromes. Leukemia & lymphoma. 2019 Dec 6;60(14):3529-35.
15. Kamvuma K, Masenga S, Hamooya B, Chanda W, Munsaka S. Prevalence and factors associated with moderate-to-severe anaemia among virally suppressed people with HIV at a tertiary hospital in Zambia. Plos one. 2024 Aug 26;19(8):e0303734.
16. Cazzola M. Ineffective erythropoiesis and its treatment. Blood, The Journal of the American Society of Hematology. 2022 Apr 21;139(16):2460-70.
17. Lyman GH, Lyman CH, Agboola O, ANC Study Group. Risk models for predicting chemotherapy-induced neutropenia. The oncologist. 2005 Jun 1;10(6):427-37.
18. Zini G. Abnormalities in leukocyte morphology and number. Blood and bone marrow pathology. 2nd ed. Philadelphia: Churchill Livingstone. 2011 Jan 1:247-61.
19. Donadieu J, Fenneteau O, Beaupain B, Mahlaoui N, Chantelot CB. Congenital neutropenia: diagnosis, molecular bases and patient management. Orphanet journal of rare diseases. 2011 Dec;6:1-28.
20. Marionneaux S. Nonmalignant leukocyte disorders. Rodak's Hematology. 2020:445.
21. De Santis GC, Brunetta DM, Vilar FC, Brandao RA, de Albernaz Muniz RZ, de Lima GM, Amorelli-Chacel ME, Covas DT, Machado AA. Hematological abnormalities in HIV-infected patients. International Journal of Infectious Diseases. 2011 Dec 1;15(12):e808-11.
22. Bhardwaj S, Almaeen A, Wani FA, Thirunavukkarasu A. Hematologic derangements in HIV/AIDS patients and their relationship with the CD4 counts: a cross-sectional study. International journal of clinical and experimental pathology. 2020;13(4):756.