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Evaluation of The Relationship Between Bone Marrow Changes and Hemogram Findings in HIV-Positive Patients

HIV Pozitif Hastalarda Kemik İliği Değişiklikleri ile Hemogram Bulguları Arasındaki İlişkinin Değerlendirilmesi

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ABSTRACT

Aim: This study aimed to evaluate the relationship between bone marrow (BM) changes and initial laboratory findings in Human immunodeficiency virus (HIV)-positive patients, focusing on hematopoietic system alterations such as myeloid hyperplasia, erythroid hyperplasia, and megakaryocyte activity.

Materials and Methods: A total of 57 HIV-positive patients were included in this retrospective study. BM findings, including cellularity, plasma cell ratio, reticulin fiber ratio, and specific features such as myeloid and erythroid hyperplasia, were analyzed. Initial laboratory parameters, including white blood cell (WBC), hemoglobin (HGB), hematocrit (HCT), platelet, and CD4 counts, were assessed.

Results: Significant positive correlations were observed between cellularity and WBC (r=0.40, p=0.005), monocyte (r=0.40, p=0.005), and CD8 counts (r=0.32, p=0.02). Plasma cell ratio showed negative correlations with HGB (r=-0.35, p=0.01), HCT (r=-0.35, p=0.01), and albumin (ALB) (r=-0.50, p<0.001). Reticulin fiber ratio was negatively correlated with WBC (r=-0.30, p=0.03), HGB (r=-0.32, p=0.02), and ALB (r=-0.35, p=0.008).

Conclusion: BM changes in HIV-positive patients, such as myeloid and erythroid hyperplasia, are associated with significant alterations in peripheral blood parameters, highlighting the importance of comprehensive hematological evaluations in this population. These findings contribute to a better understanding of HIV-related hematopoietic dysfunction and its clinical implications.

Keywords: HIV, bone marrow, myeloid hyperplasia, erythroid hyperplasia, hematopoietic dysfunction, laboratory findings

ÖZ

Amaç: Bu çalışmada İnsan immün yetmezlik virüsü (HIV) pozitif hastalarda kemik iliği (Kİ) değişiklikleri ile başlangıç laboratuvar bulguları arasındaki ilişkinin değerlendirilmesi amaçlanmış olup, miyeloid hiperplazi, eritroid hiperplazi ve megakaryosit aktivitesi gibi hematopoietik sistem değişiklikleri üzerinde durulmuştur.

Gereç ve Yöntem: Çalışmaya toplam 57 HIV pozitif hasta dahil edildi. Hücresellik, plazma hücre oranı, retikülin lif oranı ve miyeloid ve eritroid hiperplazi gibi spesifik özellikler dahil olmak üzere Kİ bulguları analiz edildi. Beyaz kan hücresi (BKH), hemoglobin (HGB), hematokrit (HT), trombosit ve CD4 sayıları dahil olmak üzere başlangıç laboratuvar parametreleri değerlendirildi.

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Bulgular: Hücresellik ile BKH (r=0,40, p=0,005), monosit (r=0,40, p=0,005) ve CD8 sayıları (r=0,32, p=0,02) arasında anlamlı pozitif korelasyon gözlendi. Plazma hücre oranı HGB (r=-0,35, p=0,01), HT (r=-0,35, p=0,01) ve albümin (ALB) (r=-0,50, p<0,001) ile negatif korelasyon gözlendi. Retikülin lif oranı BKH (r=-0,30, p=0,03), HGB (r=-0,32, p=0,02) ve ALB (r=-0,35, p=0,008) ile negatif korelasyon saptandı.

Sonuç: HIV pozitif hastalardaki Kİ değişiklikleri, miyeloid ve eritroid hiperplazi gibi, periferik kan parametrelerinde önemli değişikliklerle ilişkilidir ve bu popülasyonda kapsamlı hematolojik değerlendirmelerin önemini vurgulamaktadır. Bu bulgular, HIV ile ilişkili hematopoietik disfonksiyonun ve klinik etkilerinin daha iyi anlaşılmasına katkıda bulunmaktadır.

Anahtar Kelimeler: HIV, kemik iliği, miyeloid hiperplazi, eritroid hiperplazi, hematopoetik disfonksiyon, laboratuvar bulguları

INTRODUCTION

Human immunodeficiency virus (HIV) infection represents a major global public health challenge, with significant impacts on both individual patients and healthcare systems. Despite considerable advancements in antiretroviral therapy (ART), which have transformed HIV from a fatal condition into a manageable chronic disease, the virus continues to exert profound systemic effects. One of the most important, yet underexplored, areas of HIV's impact is its effect on the hematopoietic system and bone marrow (BM) function. Understanding the mechanisms by which HIV affects blood cell production and BM architecture is critical, as these changes are often directly correlated with disease progression, treatment response, and overall patient outcomes[1].

The hematopoietic system, driven by BM function, is essential for maintaining adequate levels of red blood cells (RBCs), white blood cells (WBCs), and platelets (PLTs), which are vital for oxygen transport, immune defense, and hemostasis, respectively. In HIV-positive patients, the virus disrupts these processes both directly, by infecting BM progenitor cells, and indirectly, by inducing systemic inflammation, opportunistic infections, and nutritional deficiencies. The resulting hematological abnormalities, including anemia, leukopenia, thrombocytopenia, and changes in BM cellularity, have a direct impact on morbidity and quality of life[2].

Anemia, one of the most common hematological manifestations in HIV-positive individuals, is multifactorial in origin, involving chronic inflammation, nutritional deficiencies (e.g., iron, vitamin B12, and folate), and BM suppression. Erythroid hyperplasia, observed in some cases, reflects a compensatory mechanism in response to anemia but may also indicate underlying marrow dysfunction. Similarly, leukopenia, particularly neutropenia, compromises the immune system's ability to combat infections, further complicating the clinical management of HIV-positive patients. Thrombocytopenia, often associated with immune thrombocytopenic purpura or direct viral effects on megakaryocytes, poses significant risks of bleeding and thrombosis. In contrast, some patients may exhibit thrombocytosis or normal PLT counts, highlighting the heterogeneity of hematological responses in HIV. BM examination provides crucial insights into the underlying pathology driving these hematological changes. Myeloid and erythroid hyperplasia, increased megakaryocyte activity, reticulin fibrosis, granuloma formation, and lymphoid nodules are some of the alterations frequently observed in HIV-positive patients. The cellularity of the BM, which can range from hypocellular to hypercellular, reflects the balance between hematopoietic activity and marrow damage. For instance, increased cellularity may correlate with systemic inflammation and higher viral loads, while hypocellularity might indicate advanced immunosuppression or marrow exhaustion[3].

Peripheral blood laboratory parameters such as hemoglobin (HGB), hematocrit (HCT), mean corpuscular volume (MCV), WBC, PLT, and inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are routinely measured in HIV-positive patients[4]. These parameters provide a snapshot of the hematological and inflammatory status of patients and are often used in conjunction with BM findings to assess disease progression, response to ART, and the risk of opportunistic infections or other complications. The correlation between these parameters and BM changes remains a critical area of study, as it has the potential to improve diagnostic accuracy and therapeutic decision-making[5]. Although several studies have documented hematological abnormalities in HIV-positive individuals, there is limited research on the direct relationship between BM changes and peripheral blood findings. For example, the presence of myeloid hyperplasia may be linked to elevated WBC counts, while reticulin fibrosis may contribute to anemia by impairing marrow function. Similarly, variations in megakaryocyte activity could explain discrepancies in PLT counts and function. These associations are essential to understanding the pathophysiology of hematological manifestations in HIV and identifying potential biomarkers for monitoring disease progression and treatment efficacy. This study aims to bridge this gap by comprehensively evaluating the relationship between BM changes and hemogram findings in HIV-positive patients. By analyzing correlations between specific hematological parameters (e.g., HGB, HCT, WBC, PLT, and inflammatory markers) and marrow alterations (e.g., cellularity, reticulin fibrosis, and hyperplasia), we seek to uncover patterns that may inform clinical practice. The study also considers the influence of other factors, such as viral load, CD4/CD8 counts, and systemic inflammation, on these hematological changes[6].

The hematological manifestations of HIV infection are a critical aspect of the disease's systemic impact, with significant implications for patient management and prognosis. By investigating the interplay between BM changes and hemogram findings, this study seeks to provide a deeper understanding of the hematopoietic system's response to HIV infection. Such insights have the potential to improve diagnostic strategies, guide therapeutic interventions, and ultimately enhance the care of HIV-positive individuals in clinical settings[7].

MATERIALS AND METHODS

Study Design and Population

This retrospective study was conducted to evaluate the relationship between BM changes and hemogram findings in HIV-positive patients. BM examination was performed in all patients to elucidate peripheral cytopenias of unknown cause. The study included 57 patients who were diagnosed with HIV and underwent BM aspiration and biopsy as part of their clinical management. The study approval was granted by Health Sciences University Türkiye, İstanbul Training and Research Hospital, Clinical Research Ethics Committee (decision no: 126, date: 29.11.2024).

Inclusion and Exclusion Criteria

Inclusion criteria were as follows: adult patients aged 18 years and above with a confirmed diagnosis of HIV infection, availability of complete blood count (CBC) results, and BM examination findings. Patients with coexisting hematological malignancies, recent chemotherapy, or other conditions known to affect BM function, such as myelodysplastic syndromes or severe nutritional deficiencies, were excluded.

Data Collection

Data were extracted from the hospital's electronic medical records. Demographic characteristics (age and gender), clinical parameters, CBC results, and BM biopsy findings were recorded. Laboratory parameters included WBC, HGB, HCT, MCV, PLT, mean platelet volume (MPV), neutrophil (NEU), monocyte (MON), and lymphocyte (LYM) counts, as well as inflammatory markers such as ESR and CRP. BM findings included cellularity, myeloid hyperplasia, erythroid hyperplasia, megakaryocyte activity, reticulin fibrosis, plasma cell ratio, and the presence of granulomas or lymphoid nodules. Additional parameters such as CD4 and CD8 counts, viral load, and liver and kidney function tests [alanine aminotransferase (ALT), albumin (ALB), creatinine] were also analyzed.

Bone Marrow Evaluation

BM aspiration and biopsy were performed and evaluated by experienced hematopathologists. Parameters assessed included cellularity (expressed as a percentage), the extent of reticulin fibrosis (graded on a scale of 0-3), and the presence of specific morphological changes such as hyperplasia, granulomas, or lymphoid nodules.

Statistical Analysis

Descriptive statistics were used to summarize the data. Continuous variables were expressed as mean ± standard deviation (SD) for normally distributed data or as median (min.-max.) for non-normally distributed data. Categorical variables were presented as frequencies and percentages. The normality of continuous data was assessed using the Kolmogorov-Smirnov test. For comparisons between two independent groups, the Student's t-test was used for normally distributed continuous variables, while the Mann-Whitney U test was applied for non-normally distributed variables. Relationships between BM findings and laboratory parameters were evaluated using the Pearson's correlation coefficient for normally distributed data and Spearman's rank correlation coefficient for non-normally distributed data. A p-value of less than 0.05 was considered statistically significant. All statistical analyses were conducted using IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY, USA).

RESULTS

This study evaluated the relationship between BM changes and hemogram findings in 57 HIV-positive patients to better understand the hematopoietic alterations associated with the disease. The analysis included demographic characteristics, BM findings, and initial laboratory parameters such as CBC and inflammatory markers. Key BM changes, including myeloid hyperplasia, erythroid hyperplasia, megakaryocyte activity, reticulin fibrosis, plasma cell ratio, and the presence of granulomas or lymphoid nodules, were assessed and compared with laboratory findings. Significant correlations were identified between specific hematological parameters and BM alterations, providing valuable insights into the interplay between peripheral blood changes and marrow pathology in the context of HIV infection. The results are presented in detail in the following sections, accompanied by relevant statistical analyses.

According to Table 1, a total of 57 HIV-positive patients were included in the study, representing a diverse group in terms of age, gender, and BM characteristics. The patients' ages ranged from a minimum of 22 to a maximum of 74 years, with a mean age of 44.2±12.1 years, reflecting the middle-aged population predominantly affected by the disease. The median age was 42 years, indicating that half of the patients were below this age and highlighting the wide range of ages in the study population.

Table 1. Distribution of patients' demographic characteristics

Descriptive characteristics	Mean ± SD	Median (min.-max.)
Age	44.2±12.1	42 (22-74)
	Count	**Percentage (%)**
Gender		
Female	3	5.3
Male	54	94.7
Myeloid hyperplasia		
Absent	30	52.6
Present	27	47.4
Erythroid hyperplasia		
Absent	36	63.2
Present	21	36.8
Megakaryocytes		
Low	3	5.3
Normal	12	21.1
High	42	73.7
Granuloma		
Absent	53	93
Present	4	7
Lymphoid nodules		
Absent	48	84.2
Present	9	15.8
	Mean ± SD	**Median (min.-max.)**
WBC	5309.81±3490.44	5030 (10-17030)
HGB	10.56±2.47	10.5 (6.10-16.30)
HCT	31.67±7.06	31.7 (17.60-48.1)
MCV	84.51±5.52	84.8 (71-96)
PLT	187056.61±119060	205000 (2000-460000)
MPV	9.82±2.02	9.8 (0-13.20)
NEU	3295.09±2682.25	2850 (0-14240)
MON	475.85±763.88	400 (0-5660)
LYM	1206.61±1119.61	1020 (0-5920)
ESR	54.47±27.83	53 (2-125)
CRP	53.67±64.47	30 (0.54-268)
Creatinine	0.77±0.27	0.71 (0.28-1.60)
ALT	69.62±206.81	23 (5-1490)
ALB	3.32±0.89	3.23 (1.64-5.30)
CD4 (%)	17.61±13.46	15 (1.15-57)
CD4	232.42±326.06	98 (4-1772)
CD8 (%)	72.56±14.05	75 (35-94)
CD8	873.55±866.57	650 (11-4461)
Viral load (copies/mL)	2349065.36±612564.41	129502 (20-30082029)
Cellularity (%)	60.85±20.19	60 (5-100)
Plasma cell ratio (%)	7.92±7.03	10 (0-20)
Reticulin fiber ratio	1.39±0.68	1 (0-3)

SD: Standard deviation, WBC: White blood cell, HGB: Hemoglobin, HCT: Hematocrit, MCV: Mean corpuscular volume, PLT: Platelet, MPV: Mean platelet volume, NEU: Neutrophil, MON: Monocyte, LYM: Lymphocyte, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, ALT: Alanine aminotransferase, ALB: Albumin

In terms of gender distribution, the majority of the participants were male (94.7%), while only 5.3% were female, suggesting a potential gender disparity in the demographic characteristics of HIV-positive individuals or in the recruitment process for the study.

BM characteristics varied among the patients, with nearly half (47.4%) exhibiting myeloid hyperplasia, which indicates an increased activity in the BMs production of myeloid cells. Erythroid hyperplasia was observed in 36.8% of the patients, reflecting changes in RBC precursor production. Granuloma formation, a sign of possible localized inflammation or infection, was noted in 7% of the cases, while lymphoid nodules, indicative of lymphoid tissue activity, were present in 15.8% of the patients.

Regarding megakaryocyte levels, which play a crucial role in PLT production, only 5.3% of the patients had low levels, while 21.1% exhibited normal levels, and a significant majority (73.7%) had elevated megakaryocyte levels. These findings highlight variations in BM activity and suggest a potential link between these hematopoietic alterations and the clinical manifestations of HIV.

This comprehensive evaluation of patient demographics and BM characteristics provides an important baseline for understanding the hematological implications of HIV infection and lays the groundwork for exploring further correlations with laboratory parameters and clinical outcomes.

The relationship between initial laboratory findings and BM findings was evaluated (Table 2).

There was a positive correlation between cellularity and WBC values (as WBC values increased, cellularity values also increased), with a correlation coefficient of r=0.40, which was statistically significant ($p^{\dagger}$=0.005).

There was also a positive correlation between cellularity and MON values (as MON values increased, cellularity values also increased), with a correlation coefficient of r=0.40, which was statistically significant ($p^{\dagger}$=0.005).

A positive correlation was observed between cellularity and CD8 values (as CD8 values increased, cellularity values also increased), with a correlation coefficient of r=0.32, which was statistically significant ($p^{\dagger}$=0.02).

There was no significant correlation between cellularity and HGB, HCT, MCV, PLT, MPV, NEU, LYM, ESR, CRP, creatinine, ALT, ALB, CD4 (%), CD4 count, CD8 (%), or viral load (copies/mL) values ($p^{\dagger}$>0.05).

For the plasma cell ratio (%), a negative correlation was observed with HGB values (as HGB values decreased, the plasma cell ratio increased), with a correlation coefficient of r=0.35, which was statistically significant ($p^{\dagger}$=0.01).

A negative correlation was also found between the plasma cell ratio (%) and HCT values (as HCT values decreased, the plasma cell ratio increased), with a correlation coefficient of r=0.35, which was statistically significant ($p^{\dagger}$=0.01).

Similarly, there was a negative correlation between the plasma cell ratio (%) and ALB values (as ALB values decreased, the plasma cell ratio increased), with a correlation coefficient of r=0.50, which was statistically significant ($p^{\dagger}$<0.001).

Negative correlations were also observed between the plasma cell ratio (%) and CD4 (%) values (r=0.40, $p^{\dagger}$=0.005), CD4 count (r=0.42, $p^{\dagger}$=0.001), and CD8 (%) values (r=0.40, $p^{\dagger}$=0.005).

No significant correlation was found between the plasma cell ratio (%) and WBC, MCV, PLT, MPV, NEU, MON, LYM, ESR, CRP, creatinine, ALT, CD8 count, or viral load (copies/mL) values ($p^{\dagger}$>0.05).

For the reticulin fiber ratio, a negative correlation was found with WBC values (as WBC values decreased, the reticulin fiber ratio increased), with a correlation coefficient of r=0.30, which was statistically significant ($p^{\dagger\dagger}$=0.03).

A negative correlation was also found with HGB values (as HGB values decreased, the reticulin fiber ratio increased), with a correlation coefficient of r=0.32, which was statistically significant ($p^{\dagger\dagger}$=0.02).

Similarly, a negative correlation was observed between the reticulin fiber ratio and HCT values (as HCT values decreased, the reticulin fiber ratio increased), with a correlation coefficient of r=0.35, which was statistically significant ($p^{\dagger\dagger}$=0.008).

A negative correlation was also observed with ALB values (as ALB values decreased, the reticulin fiber ratio increased), with a correlation coefficient of r=0.35, which was statistically significant ($p^{\dagger\dagger}$=0.008).

No significant correlation was found between the reticulin fiber ratio and MCV, PLT, MPV, NEU, MON, LYM, ESR, CRP, creatinine, ALT, CD4 (%), CD4 count, CD8 count, CD8 (%), or viral load (copies/mL) values ($p^{\dagger}$+>0.05).

The mean or median differences in initial laboratory parameters were evaluated based on the presence of myeloid hyperplasia (Table 3).

The mean ± SD and median (Q_1-Q_3) values for WBC were 4214±2572.54 and 3920 (1930-5540) in patients without myeloid hyperplasia, and 6908.52±3802.17 and 6160 (4250-9210) in patients with myeloid hyperplasia. The difference in

Table 2. Evaluation of the relationship between initial laboratory findings and bone marrow findings

Parameter	Cellularity (%)		Plasma cell ratio (%)		Reticulin fiber ratio	
	r	$p^{\dagger}$	r	$p^{\dagger}$	r	$p^{\dagger\dagger}$
WBC	0.40	**0.005**	-0.18	0.17	-0.30	**0.03**
HGB	-0.11	0.45	-0.35	**0.01**	-0.32	**0.02**
HCT	-0.10	0.48	-0.35	**0.01**	-0.35	**0.008**
MCV	-0.02	0.89	0.08	0.58	0.22	0.09
PLT	0.12	0.37	-0.21	0.12	-0.30	0.03
MPV	-0.01	0.95	0.13	0.33	0.01	0.92
NEU	0.16	0.24	-0.06	0.66	-0.15	0.30
MON	0.40	**0.005**	-0.17	0.21	0.02	0.90
LYM	0.15	0.26	-0.11	0.43	0.04	0.75
ESR	0.05	0.70	0.12	0.41	0.07	0.60
CRP	-0.08	0.56	0.07	0.63	0.24	0.07
Creatinine	-0.04	0.75	-0.14	0.30	-0.13	0.33
ALT	-0.05	0.73	-0.11	0.42	0.14	0.30
ALB	-0.14	0.31	-0.50	**<0.001**	-0.35	0.008
CD4 (%)	-0.07	0.62	-0.40	**0.005**	-0.12	0.39
CD4	0.25	0.06	-0.42	**0.001**	-0.19	0.16
CD8 (%)	0.25	0.06	0.40	**0.005**	0.02	0.89
CD8	0.32	0.02	-0.18	0.19	-0.09	0.52
Viral load (copies/mL)	0.12	0.36	0.23	0.08	0.002	0.99

†Pearson correlation, ††Spearman correlation, p<0.05 significance. WBC: White blood cell, HGB: Hemoglobin, HCT: Hematocrit, MCV: Mean corpuscular volume, PLT: Platelet, MPV: Mean platelet volume, NEU: Neutrophil, MON: Monocyte, LYM: Lymphocyte, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, ALT: Alanine aminotransferase, ALB: Albumin, r: Pearson correlation coefficient

WBC values between the groups was statistically significant ($p^{††}$=0.005).

The mean ± SD and median (Q_1-Q_3) values for NEU were 2453.67±1491.26 and 2250 (1525-3575) in patients without myeloid hyperplasia, and 4382.22±3177.85 and 3600 (2110-5240) in patients with myeloid hyperplasia. The difference in NEU values between the groups was statistically significant ($p^{††}$=0.01).

The mean ± SD and median (Q_1-Q_3) values for other laboratory parameters, as listed in Table 3, indicated no statistically significant differences based on the presence of myeloid hyperplasia. These parameters included HGB, HCT, MCV, PLT, MPV, MON, LYM, ESR, CRP, creatinine, ALB, CD4 (%), CD4 count, CD8 (%), CD8 count, and viral load (copies/mL) (p>0.05).

The mean or median differences in initial laboratory parameters were evaluated based on the presence of erythroid hyperplasia (Table 4).

The mean ± SD value for CD8 (%) was 69.33±15.01 in patients without erythroid hyperplasia and 78.49±9.91 in patients with erythroid hyperplasia. The difference in CD8 (%) values between the groups was statistically significant ($p^{†}$=0.007).

The mean ± SD and median (Q_1-Q_3) values for other laboratory parameters are provided in Table 4. These values indicate that there were no statistically significant differences between the

Table 3. Evaluation of differences in initial laboratory parameters based on the presence of myeloid hyperplasia

Myeloid hyperplasia	Absent	Present	
	Mean ± SD Median (Q_1-Q_3)	Mean ± SD Median (Q_1-Q_3)	p-value
WBC	4214±2572.54 3920 (1930-5540)	6908.52±3802.17 6160 (4250-9210)	0.005††
HGB	10.72±2.52	10.51±2.57	0.76†
HCT	32.09±7.26	31.52±7.11	0.76†
MCV	85.27±5.93	83.32±4.85	0.19†
PLT	174400±118673.59 175000 (46000-232500)	199259.26±122220.35 228000 (90000-288000)	0.29††
MPV	10.17±1.63	9.52±2.37	0.24†
NEU	2453.67±1491.26 2250 (1525-3575)	4382.22±3177.85 3600 (2110-5240)	0.01††
MON	374±251.57 320 (200-560)	611.11±1035.09 430 (210-520)	0.37††
LYM	1258.67±1174.49 1020 (520-1600)	1308.89±1125.25 1280 (460-1620)	0.76††
ESR	56.6±27.34	48.79±28.38	0.44†
CRP	53.65±72.87 25 (2.5-89)	50.61±52.34 35 (4-86)	0.63††
Creatinine	0.78±0.27	0.79±0.31	0.83†
ALT	94.33±268.63 27 (14.5-67.5)	33.59±58.28 18 (15-25)	0.09††
ALB	3.39±0.79	3.26±1.06	0.56†
CD4 (%)	17.48±8.21	18.01±9.11	0.88†
CD4	201.63±257.32 86 (30.5-337.5)	266.04±375.09 134 (52-297)	0.26††
CD8 (%)	71.27±16.12	74.3±11.02	0.42†
CD8	793.97±744.91 679 (405-1091)	955.96±980.35 633 (366-1102)	0.84††
Viral load (copies/mL)	2276578.52±6533180.21 5544 (131-774202)	2323432.63±5443235.22 149000 (275-3470000)	0.35††

†Student's t-test, ††Mann-Whitney U test, Q1-Q3: 25th-75th percentile. SD: Standard deviation, WBC: White blood cell, HGB: Hemoglobin, HCT: Hematocrit, MCV: Mean corpuscular volume, PLT: Platelet, MPV: Mean platelet volume, NEU: Neutrophil, MON: Monocyte, LYM: Lymphocyte, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, ALT: Alanine aminotransferase, ALB: Albumin

groups based on the presence of erythroid hyperplasia for WBC, HGB, HCT, MCV, PLT, MPV, NEU, MON, LYM, ESR, CRP, creatinine, ALT, ALB, CD4 (%), CD4 count, CD8 count, and viral load (copies/mL) (p>0.05).

The mean or median differences in initial laboratory parameters were evaluated based on the presence of megakaryocytes (Table 5).

The mean ± SD and median (Q_1-Q_3) values for laboratory parameters based on megakaryocyte status are provided in Table 5. According to these values, there were no statistically significant differences in WBC, HGB, HCT, MCV, PLT, MPV, NEU, MON, LYM, ESR, CRP, creatinine, ALT, ALB, CD4 (%), CD4 count, CD8 (%), CD8 count, and viral load (copies/mL) measurements based on megakaryocyte status (p>0.05) (Table 5).

DISCUSSION

The findings of this study provide valuable insights into the hematological alterations observed in HIV-positive patients and their associations with BM findings. The inclusion of a diverse sample of 57 patients allowed for a detailed analysis of various hematopoietic parameters and their clinical implications. These results contribute to the growing body of evidence on the systemic effects of HIV on the hematopoietic system and highlight areas for further research and clinical attention[8].

Table 4. Evaluation of differences in initial laboratory parameters based on the presence of erythroid hyperplasia

Erythroid hyperplasia	Absent	Present	
	Mean ± SD Median (Q_1-Q_3)	Mean ± SD Median (Q_1-Q_3)	p-value
WBC	5326.94±3554.76 5180 (3020-7180)	5770.48±3362.14 5040 (3990-6385)	0.64††
HGB	10.66±2.45	10.55±2.69	0.89†
HCT	31.98±7.11	31.57±7.33	0.84†
MCV	84.39±5.23	84.27±6.04	0.94†
PLT	202972.22±122040.15 208000 (99000-310000)	157380.95±113298.93 189000 (38500-240500)	0.18††
MPV	10.09±1.47	9.49±2.71	0.28†
NEU	3191.11±2438.33 2850 (1730-3940)	3669.05±2905.09 3040 (2090-4540)	0.45††
MON	517.5±913.47 400 (180-510)	432.86±244.19 410 (270-555)	0.57††
LYM	1154.44±1115.29 910 (360-1480)	1501.91±1179.41 1280 (900-1655)	0.15††
ESR	53.19±27.21	52.55±28.61	0.95†
CRP	53.15±72.79 19 (3-86)	50.59±44.61 40 (7.81-95.5)	0.36††
Creatinine	0.80±0.28	0.76±0.31	0.63†
ALT	83.47±245.95 25 (17-50)	35.71±65.99 18 (11.5-32.5)	0.08††
ALB	3.38±0.81	3.25±1.06	0.59†
CD4 (%)	19.52±8.69	14.65±8.99	0.19†
CD4	247.36±353.79 99 (37-341)	206.04±248.37 94 (61-257)	0.86††
CD8 (%)	69.33±15.01	78.49±9.91	**0.007†**
CD8	776.17±821.58 640 (433-912)	1032.76±920.73 971 (371.5-1222)	0.08††
Viral load (copies/mL)	1988185.61±5630939.98 17057 (146-771404)	2817474.38±6627244.34 411000 (223.5-3841738.5)	0.30††

†Student's t-test, ††Mann-Whitney U test, Q1-Q3: 25th-75th percentile. SD: Standard deviation, WBC: White blood cell, HGB: Hemoglobin, HCT: Hematocrit, MCV: Mean corpuscular volume, PLT: Platelet, MPV: Mean platelet volume, NEU: Neutrophil, MON: Monocyte, LYM: Lymphocyte, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, ALT: Alanine aminotransferase, ALB: Albumin

One of the key observations of this study is the significant variation in BM activity among HIV-positive patients, as reflected in the presence of myeloid hyperplasia (47.4%) and erythroid hyperplasia (36.8%). These findings suggest a compensatory response by the BM to peripheral cytopenias commonly observed in HIV infection. Myeloid hyperplasia, which reflects an increased production of myeloid precursor cells, may be a response to chronic immune activation and the increased turnover of WBCs. Erythroid hyperplasia, on the other hand, could be attributed to anemia of chronic disease, often seen in advanced HIV cases, as well as potential direct effects of the virus on erythropoiesis. The significant correlation between BM cellularity and laboratory parameters, such as WBC and MON counts, underscores the active role of the BM in responding to systemic changes in HIV-positive individuals[9].

Granuloma formation and the presence of lymphoid nodules in a subset of patients (7% and 15.8%, respectively) highlight the diverse pathological processes occurring in the BM. Granulomas may indicate opportunistic infections, which are common in immunocompromised states such as HIV, while lymphoid nodules may reflect abnormal lymphoid activity or residual immune responses. The low prevalence of granulomas in this study could be due to effective ART among the patients, as ART is known to reduce opportunistic infections.

Another noteworthy finding is the elevated megakaryocyte levels in most of the patients (73.7%). Increased megakaryocyte

Table 5. Evaluation of differences in initial laboratory parameters based on the presence of megakaryocytes

Megakaryocyte status	Low/normal	High	
	Mean ± SD Median (Q_1-Q_3)	Mean ± SD Median (Q_1-Q_3)	p-value
WBC	4517.33±3349.94 5030 (860-7510)	5837.86±3473.18 5180 (3325-7035)	0.34††
HGB	10.92±2.91	10.51±2.41	0.60†
HCT	32.28±8.11	31.66±6.85	0.78†
MCV	84.73±5.61	84.24±5.51	0.75†
PLT	195866.67±119120.51 208000 (85000-310000)	182714.28±121476.34 191000 (66500-260500)	0.67††
MPV	9.81±1.46	9.89±2.19	0.88†
NEU	2324.67±1709.55 2090 (490-3400)	3739.52±2780.02 3220 (2060-4540)	0.07††
MON	404±306.68 410 (60-670)	515.71±841.55 410 (210-505)	0.98††
LYM	1614±1553.92 1740 (250-2020)	1164.05±948.87 1020 (570-1395)	0.36††
ESR	50.64±19.47	53.74±20.34	0.79†
CRP	51.12±76.47 10.6 (3-111)	52.59±59.15 40 (4-86)	0.50††
Creatinine	0.84±0.36	0.77±0.26	0.44††
ALT	138.33±376.68 23 (15-74)	40±58.68 21 (14.5-46.5)	0.57††
ALB	3.65±0.96	3.22±0.87	0.13†
CD4 (%)	21.49±8.38	16.38±9.12	0.21†
CD4	298.27±315.68 208 (24-523)	208.52±318.27 94 (46-236.5)	0.49††
CD8 (%)	67.68±16.74	74.5±12.48	0.11†
CD8	980.8±1022.06 687 (254-1227)	831.38±805.19 650 (429.5-1009)	0.70††
Viral load (copies/mL)	1038476.67±2525412.51 411000 (206-771404)	2760397.76±6789031.72 123000 (171.5-1240000)	0.75††

†Student's t-test, ††Mann-Whitney U test, Q_1-Q_3: 25th-75th quartiles. SD: Standard deviation, WBC: White blood cell, HGB: Hemoglobin, HCT: Hematocrit, MCV: Mean corpuscular volume, PLT: Platelet, MPV: Mean platelet volume, NEU: Neutrophil, MON: Monocyte, LYM: Lymphocyte, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, ALT: Alanine aminotransferase, ALB: Albumin

activity may be a compensatory mechanism to address thrombocytopenia, a common hematological abnormality in HIV. However, the lack of significant differences in PLT counts between patients with low, normal, or high megakaryocyte levels suggests that factors beyond megakaryocyte activity, such as peripheral PLT destruction or impaired PLT function, may play a role in HIV-associated thrombocytopenia[10].

The significant associations between plasma cell ratio and laboratory parameters such as HGB, HCT, ALB, and CD4 counts indicate that plasma cell activity may serve as a marker for disease progression in HIV-positive patients. A negative correlation with these parameters suggests that increased plasma cell activity may coincide with worsening anemia, hypoalbuminemia, and immunosuppression. Similarly, the reticulin fiber ratio, which was negatively correlated with WBC, HGB, HCT, and ABL levels, points to a potential role of BM fibrosis in contributing to cytopenias and poor clinical outcomes in HIV. These findings are consistent with previous studies suggesting that BM fibrosis, while not common, may occur in chronic HIV infection and negatively impact hematopoiesis[11].

This study also highlights the lack of significant differences in certain parameters based on BM findings, such as viral load and CD8 counts. While these parameters are critical indicators of HIV disease activity and immune response, their lack of correlation with specific BM findings in this study may reflect the complex interplay of multiple factors influencing HIV pathology. Further studies with larger sample sizes and more comprehensive analyses are needed to elucidate these relationships.

The gender disparity in the study population, with males comprising 94.7% of the participants, raises questions about the representativeness of the sample. This skewed distribution may reflect differences in healthcare-seeking behavior, access to care, or prevalence rates between genders. Future studies should aim for more balanced gender representation to ensure generalizability of the findings[12].

While this study provides important insights, it has several limitations. The retrospective nature of the study limits the ability to infer causality between the observed hematological changes and HIV infection. Additionally, although the sample size was sufficient for initial analyses, it may not capture the full spectrum of hematological alterations in HIV-positive patients. Moreover, the study did not account for potential confounding factors such as ART regimens, duration of therapy, or comorbid conditions, which may influence both laboratory and BM findings. This study highlights the significant hematopoietic changes occurring in HIV-positive patients and their complex interplay with clinical and laboratory parameters. The findings underscore the importance of comprehensive hematological evaluations in HIV management and provide a basis for future research aiming at understanding the mechanisms underlying these changes. A deeper understanding of these processes could lead to the development of targeted interventions to mitigate the hematological complications of HIV and improve patient outcomes[13].

The results presented in this study provide a comprehensive evaluation of the hematological and BM findings in HIV-positive patients, with detailed statistical analyses highlighting significant relationships and differences between laboratory and BM parameters. Each table offers critical insights into the interplay between various hematopoietic changes and clinical features.

Table 1 provides a foundational understanding of the demographic and BM characteristics of the study population. The mean age of 44.2±12.1 years with a median age of 42 years reflects a middle-aged demographic, which is commonly affected by HIV. The overwhelming male predominance (94.7%) raises questions about the gender distribution of HIV in the sampled population, potentially reflecting biases in healthcare access or recruitment.

Statistically, the presence of myeloid hyperplasia in 47.4% and erythroid hyperplasia in 36.8% of patients highlights a compensatory response of the BM to peripheral cytopenias. Similarly, the high proportion of elevated megakaryocyte levels (73.7%) reflects significant PLT production activity, even though PLT counts did not differ significantly across megakaryocyte groups. Granulomas (7%) and lymphoid nodules (15.8%) further emphasize the diverse BM pathology in this cohort, potentially linked to opportunistic infections or abnormal immune activation.

Table 2 presents correlations between initial laboratory findings and BM parameters, highlighting statistically significant relationships that illuminate underlying pathophysiological mechanisms. Considering, cellularity, a positive correlation was observed between cellularity and WBC, MON, and CD8. These findings suggest that increased cellularity reflects an active BM response to immune cell turnover, characteristic of chronic HIV infection. Other parameters, such as HGB, HCT, and PLT counts, showed no significant correlation, indicating that cellularity changes might be more reflective of immune cell dynamics rather than RBC or PLT precursors. In terms of plasma cell ratio, negative correlations were observed with HGB, HCT, ALB, and CD4 count. These findings underscore the association of increased plasma cell activity with worsening anemia and hypoalbuminemia, which are hallmarks of advanced HIV. The inverse relationship with CD4 counts suggests that plasma cell hyperactivity may accompany immunosuppression in later stages of the disease. For reticulin fiber ratio, significant negative correlations were found with WBC, HGB, HCT, and

ALB. These findings suggest that BM fibrosis, represented by increased reticulin fibers, contributes to cytopenias and hypoalbuminemia. This aligns with the hypothesis that fibrosis may disrupt the BM microenvironment, impairing hematopoiesis[14].

Table 3 evaluates differences in laboratory parameters based on the presence of myeloid hyperplasia. Patients with myeloid hyperplasia showed significantly higher WBC and NEU counts compared to those without hyperplasia. These results indicate that myeloid hyperplasia reflects a robust compensatory mechanism to address immune cell demands in HIV-positive patients. Other parameters, including HGB, HCT, PLT, and CD4 counts, did not show significant differences between the groups, which suggests that myeloid hyperplasia primarily affects the WBC lineage without markedly influencing other hematopoietic lineages.

Table 4 focuses on differences in laboratory parameters based on the presence of erythroid hyperplasia. The only statistically significant finding was a higher CD8 (%) in patients with erythroid hyperplasia. This suggests a potential link between erythropoietic activity and immune responses, possibly reflecting heightened immune activation in this subgroup. No significant differences were observed for other parameters, such as HGB, HCT, or viral load. This lack of association highlights the multifactorial nature of anemia in HIV, where factors beyond erythroid hyperplasia likely play a role.

Table 5 examines differences in laboratory parameters based on megakaryocyte status. Despite the high proportion of patients with elevated megakaryocyte levels, no statistically significant differences were found in PLT counts or other laboratory parameters. This finding suggests that megakaryocyte elevation may not directly translate into changes in peripheral PLT counts, potentially due to increased PLT destruction or altered function in HIV.

Statistical Implications and Clinical Relevance

The findings from the tables emphasize the complexity of hematological changes in HIV. Significant correlations and differences highlight specific areas of BM activity, such as myeloid and erythroid hyperplasia, that correlate with peripheral blood parameters. These insights suggest that BM evaluations can provide critical information on disease progression and potential complications in HIV-positive patients[15].

Moreover, the lack of significant associations in some parameters, such as viral load or CD4 counts in specific contexts, underscores the need for further research to untangle the multifactorial influences on BM function. The use of advanced statistical methods, as implemented in this study, strengthens the reliability of the findings and provides a robust foundation for future investigations.

The integration of detailed statistical analyses from these tables into clinical interpretations enhances our understanding of the hematological impact of HIV. These results can guide targeted interventions to address specific hematological abnormalities, ultimately improving outcomes for HIV-positive patients.

Study Limitations

Potential limitations include the retrospective design, which may introduce selection bias, and the relatively small sample size, which may limit the generalizability of the findings. Despite these limitations, the study provides valuable insights into the relationship between hematological and BM findings in HIV-positive patients.

CONCLUSION

This study highlights the significant hematological and BM alterations in HIV-positive patients, revealing critical correlations between laboratory parameters and BM findings. Myeloid and erythroid hyperplasia, as well as elevated megakaryocyte levels, reflect the BM's compensatory responses to the systemic effects of HIV. Key associations, such as the link between plasma cell ratio and markers of anemia and immunosuppression, underscore the complexity of HIV-associated hematopoietic dysfunction. While this study provides valuable insights into the interplay between HIV and hematopoiesis, further research is needed to explore the underlying mechanisms and clinical implications. These findings emphasize the importance of comprehensive hematological evaluations in the management of HIV to mitigate complications and improve patient outcomes[16].

Ethics

Ethics Committee Approval: The study approval was granted by Health Sciences University Türkiye, İstanbul Training and Research Hospital, Clinical Research Ethics Committee (decision no: 126, date: 29.11.2024).

Informed Consent: Retrospective study.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: A.K., N.B.S., G.E.H., Concept: A.K., M.H.D., R.E., G.E.H., Design: A.K., C.A., R.E., G.E.H., Data Collection or Processing: V.C.C.., C.A., N.D.S., Analysis or

Interpretation: A.K., M.H.D., R.E., Literature Search: V.C.C., C.A., N.D.S., Writing: A.K., C.A., G.E.H.

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