

Hematological Profiles of Newly Diagnosed HIV Patients Initiated on Dolutegravir-Based Therapy at the University of Nigeria Teaching Hospital, Enugu

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Received date: June 12, 2025, **Accepted date:** August 05, 2025

Citation: Onwuka-Kalu CO, Chukwurah EF, Ukwah BN, Usanga VU, Appiah SK, Nkansah C. Hematological Profiles of Newly Diagnosed HIV Patients Initiated on Dolutegravir-Based Therapy at the University of Nigeria Teaching Hospital, Enugu. J Clin Haematol. 2025;6(1):83–88.

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Abstract

Background: Dolutegravir (DTG), an integrase strand transfer inhibitor, is increasingly adopted as the preferred first-line antiretroviral therapy (ART) due to its potent virological efficacy and high barrier to resistance. However, emerging safety concerns—such as reports of neural tube defects, neuropsychiatric symptoms, and hematological abnormalities including sideroblastic anemia—have raised important questions regarding its long-term safety profile.

Objective: This study assessed the impact of initiating DTG-based ART on hematological parameters—including red blood cell indices, white blood cell differentials, and platelet indices—among treatment-naïve HIV-positive individuals.

Methods: A total of 40 treatment-naïve HIV-positive adults (19 males, 21 females) without co-morbidities were prospectively recruited from the Antiretroviral Therapy Clinic of the University of Nigeria Teaching Hospital (UNTH), Enugu, between January 2023 and July 2024. Forty age- and sex-matched HIV-seronegative individuals served as controls. Baseline socio-demographics were collected using a structured questionnaire. Blood samples were obtained at baseline and after six months of DTG-based ART initiation. Complete blood count (CBC) was assessed using an automated hematology analyzer.

Results: After six months of DTG-based ART, statistically significant hematological changes were observed. These included increases in red blood cell count ($4.78 \pm 0.49 \times 10^{12}/L$), hemoglobin concentration (13.82 ± 1.55 g/dL), hematocrit level ($40.61 \pm 3.91\%$), mean corpuscular volume (82.22 ± 4.84 fL), mean corpuscular hemoglobin (26.27 ± 1.97 pg), and neutrophil count ($51.53 \pm 8.94\%$). Conversely, a decrease in lymphocyte count ($35.47 \pm 7.81\%$) was noted. No significant changes were observed in mean corpuscular hemoglobin concentration (MCHC), red cell distribution width–coefficient of variation (RDW-CV), or red cell distribution width–standard deviation (RDW-SD).

Conclusion: DTG-based ART was associated with significant changes in several hematological indices and anthropometric parameters after six months of treatment. These findings underscore the importance of continued hematologic monitoring and long-term safety assessment in patients receiving DTG-containing regimens.

Keywords: Hematology, Dolutegravir, Red cell indices, Platelet indices, White blood cells count, HIV, Antiretroviral therapy (ART), Sub-Saharan Africa

Introduction

Human Immunodeficiency Virus (HIV) infection continues to pose a major global public health challenge, with sub-Saharan Africa bearing a disproportionate share of the burden. According to UNAIDS [1], the region accounts for nearly two-thirds of the global HIV population, underscoring the urgent need for effective and sustainable treatment strategies. The advent and evolution of antiretroviral therapy (ART) have significantly reduced HIV-related morbidity and mortality, transforming the disease into a manageable chronic condition for many individuals [2,3]. Among recent advances in ART, dolutegravir (DTG)—a second-generation integrase strand transfer inhibitor (INSTI)—has emerged as a preferred first-line agent due to its potent virological efficacy, high genetic barrier to resistance, and once-daily dosing convenience [4,5].

Despite its favorable pharmacological profile, increasing clinical use of DTG-based regimens has prompted concerns regarding their long-term safety, particularly in relation to hematological, metabolic, and neurodevelopmental outcomes [6,7]. These concerns are especially relevant in low-resource settings, where baseline nutritional deficiencies and co-infections may amplify drug-related adverse effects.

HIV infection is frequently associated with weight loss, malnutrition, and micronutrient deficiencies—notably of iron and folate—which are essential for effective erythropoiesis and immune function. These deficiencies, along with direct viral suppression of hematopoietic progenitor cells and bone marrow dysfunction, contribute to a wide range of hematological abnormalities, including anemia, leukopenia, and thrombocytopenia [8]. Such abnormalities are among the earliest and most consistent complications in people living with HIV (PLWH), often serving as prognostic markers for disease progression and therapeutic outcomes [9,10].

Anemia is the most prevalent hematological manifestation in HIV, strongly associated with advanced immunosuppression, chronic inflammation, nutritional deficiencies, and opportunistic infections [11]. Its etiology is multifactorial, including impaired bone marrow response, cytokine dysregulation, and decreased erythropoietin production. Similarly, leukopenia—particularly neutropenia and lymphopenia—arises from both direct viral effects and immune dysregulation, increasing susceptibility to bacterial, fungal, and viral infections [12]. Thrombocytopenia may result from immune-mediated platelet destruction, marrow suppression, or ART-related toxicity, and has been linked with increased bleeding risk and delayed wound healing [13].

Given that ART itself may influence hematological profiles—either through viral suppression or potential marrow toxicity—the need for ongoing evaluation of hematologic safety profiles of newer ART regimens, including DTG-based therapies, becomes imperative. Monitoring complete blood

count (CBC), along with iron and folate levels, provides essential diagnostic and prognostic information in HIV care, particularly in resource-limited settings where advanced laboratory investigations may not be readily available [14,15].

In Nigeria, where DTG-based ART has been widely adopted as the preferred first-line regimen, data on its hematological impact remain scarce. Given the influence of ART on hematological profiles—either through viral suppression or potential marrow toxicity—and in light of baseline nutritional and health disparities, there is a growing need to assess how DTG affects key hematological indices among HIV-infected individuals in this context. This study assessed the impact of initiating DTG-based ART on hematological parameters—including red blood cell indices, white blood cell differentials, and platelet indices—among treatment-naïve HIV-positive individuals in Enugu, Nigeria, thereby contributing to the broader understanding of its safety and clinical implications within sub-Saharan Africa. Such findings are expected to inform patient monitoring protocols, optimize therapeutic outcomes, and support evidence-based policymaking in HIV management.

Materials and Methods

Study design and participants

This study was a cross-sectional, analytical investigation involving people living with HIV (PLWH) receiving medical care in Enugu, Nigeria. Participants included newly diagnosed HIV-positive individuals who had not initiated ART and had no co-morbid conditions, as well as HIV-negative controls without significant health issues. Exclusion criteria comprised prior exposure to ART, refusal to provide consent, or presence of known HIV-related co-morbidities. Ethical approval was obtained from the University of Nigeria Teaching Hospital Research Ethical Committee and written informed consent was secured from all participants prior to sample collection.

Complete blood count (CBC) analysis

Complete blood count (CBC) parameters were determined using the *Zybio Z31 Automated Hematology Analyzer*, which operates on the Coulter principle. The analyzer quantifies cellular components by detecting changes in electrical resistance as cells suspended in an electrolyte solution pass through a narrow aperture. Each blood cell, when passing through the aperture, causes a momentary impedance (electrical resistance) change that is measured as an electrical pulse. The amplitude of this pulse is directly proportional to the cell's volume, allowing for differentiation and enumeration of red blood cells (RBCs), white blood cells (WBCs), and platelets (PLTs). For hemoglobin determination, the analyzer employs a colorimetric method. Upon addition of a lyse reagent, erythrocyte membranes are disrupted,

releasing hemoglobin. The hemoglobin forms a chromogenic complex that is detected at a wavelength of 525 nm using an LED monochromatic light source. The transmitted light is measured by a photocell, and the resulting signal is amplified and analyzed against a baseline diluent reading to determine hemoglobin concentration. All measurements were performed according to the manufacturer’s instructions and in adherence to standard laboratory protocols [16].

Data management and statistical analysis

All data were coded and securely stored in a password-protected computer system. Each sample was assigned a unique laboratory identification number to ensure anonymity during processing and analysis. Personal identifiers such as names, contact details, and clinical histories were excluded from analytical datasets.

Data analysis was conducted using the Statistical Package for Social Sciences (SPSS) version 26.0 for Windows. Descriptive statistics (means, standard deviations, frequencies, and percentages) were used to summarize continuous and categorical variables. Differences in continuous variables between groups were assessed using Student’s t-test, while the Chi-square test was employed for categorical data. A p-value of less than 0.05 was considered statistically significant. Results are presented using tables and graphical illustrations where appropriate.

Confidentiality and data protection

Participant confidentiality was strictly maintained throughout the study. All personal information, including age and contact details, was anonymized and securely stored. Laboratory results were identified solely by coded numbers and were communicated individually to each participant following analysis.

Results

Table 1 shows that the age groups are significantly different between the subjects and controls ($\chi^2=20.254$, $p<0.001$). The mean age is 37.32 ± 8.63 , the minimum age is 19 while the maximum age is 53 years. There are 37.8% of the subjects aged between 39–48 years compared to 13.5% of controls within the age bracket. Conversely, there are 16.2% of the subjects aged between 19–28 years compared to 64.9% of controls within the age bracket. However, the gender proportions of both groups are not significantly different ($\chi^2=0.054$, $p=0.816$). There are 48.6% and 51.4% male subjects and controls respectively. Majority of the subjects and controls have secondary education ($\chi^2=0.670$, $p=0.715$), while over 70% of participants in both groups are in the low socioeconomic class ($\chi^2=1.019$, $p=0.601$). The subjects were predominantly business/traders (56.8%) compared to the controls that are predominantly civil servants (45.9%), ($\chi^2=20.567$, $p=0.001$).

Table 1. Socio-demographic characteristics of study participants.				
Variable	Subjects n (%)	Controls n (%)	χ²	p-value
Age Group (years)				
19–28	6 (16.2)	24 (64.9)	20.254	< 0.001
29–38	13 (35.1)	8 (21.6)		
39–48	14 (37.8)	5 (13.5)		
49–58	4 (10.8)	0 (0.0)		
Sex				
Male	18 (48.6)	19 (51.4)	0.054	0.816
Female	19 (51.4)	18 (48.6)		
Educational Status				
Primary	10 (27.0)	10 (27.0)	0.670	0.715
Secondary	16 (43.2)	13 (35.1)		
Tertiary	11 (29.7)	14 (37.8)		
Socioeconomic Status				
Low	27 (73.0)	26 (70.3)	1.019	0.601
Middle	10 (27.0)	10 (27.0)		
High	0 (0.0)	1 (2.7)		

Occupation				
Artisan	7 (18.9)	0 (0.0)	20.567	0.001
Business/Trader	21 (56.8)	14 (37.8)		
Civil Servant	7 (18.9)	17 (45.9)		
Farmer	0 (0.0)	3 (8.1)		
Student	0 (0.0)	3 (8.1)		
Unemployed	2 (5.4)	0 (0.0)		
Marital Status				
Single	14 (37.8)	18 (48.6)	0.881	0.348
Married	23 (62.2)	19 (51.4)		

Following six months of DTG-based ART, people living with HIV (PLWH) demonstrated significant improvements in key hematological parameters, including increases in hemoglobin, hematocrit, red blood cell count, MCV, and MCH, indicating enhanced erythropoiesis. Despite these gains, most red cell indices remained significantly lower than in HIV-negative controls. White blood cell counts showed no significant overall change, but neutrophil levels increased significantly while lymphocyte levels declined post-treatment, reflecting a shift in immune profile. Platelet indices, including platelet count, PCT, PDW, and MPV, exhibited non-significant changes post-

ART and remained within normal ranges, suggesting a stable thrombopoietic response. Overall, DTG-based therapy led to partial normalization of hematological parameters, though some disparities with controls persisted.

Discussion

The hematological profile of people living with HIV (PLWH) offers valuable insights into disease progression, immune status, and therapeutic response. In this study, significant improvements were observed in several hematological

Table 2. Mean hematological parameters of treatment-naïve, treatment-experienced (Post-DTG), and control subjects.						
Parameter	Pre-DTG (Mean±SD)	Post-DTG (Mean±SD)	Control (Mean±SD)	p (t-test)	p (Pre vs Control)	p (Post vs Control)
Hemoglobin (g/dL)	11.13±1.87	13.82±1.55	14.85±1.33	0.000	<0.001	<0.01
Hematocrit (%)	33.26±4.52	40.61±3.91	44.23±2.87	0.000	<0.001	<0.01
MCV (fL)	74.45±6.10	82.22±4.84	86.79±3.92	0.000	<0.001	<0.05
MCH (pg)	23.11±2.15	26.27±1.97	28.35±1.84	0.000	<0.001	<0.01
MCHC (g/dL)	31.15±1.13	31.68±1.08	32.65±1.01	0.188	<0.001	<0.05
RDW-CV (%)	13.70±1.22	13.17±1.05	12.35±0.88	0.714	<0.05	<0.01
RDW-SD (fL)	38.10±2.75	37.24±2.46	35.42±2.30	0.377	<0.001	<0.01
RBC (×10 ¹² /L)	4.28±0.52	4.78±0.49	4.28±0.47	0.023	0.950	<0.01
WBC (×10 ⁹ /L)	5.43±1.26	6.18±1.41	5.80±1.17	0.358	0.304	0.601
Lymphocytes (%)	46.37±8.53	35.47±7.81	40.92±6.72	0.001	<0.01	<0.05
Neutrophils (%)	40.18±9.26	51.53±8.94	51.53±7.89	0.001	<0.001	1.000
Monocytes (%)	7.98±1.74	7.72±1.65	7.72±1.55	0.531	<0.05	1.000
Platelet Count (×10 ⁹ /L)	222.72±45.87	253.77±52.63	253.77±48.92	0.267	0.012	1.000
PCT (%)	0.231±0.043	0.247±0.041	0.247±0.037	0.201	0.108	1.000
PDW (fL)	15.85±0.92	15.74±0.89	15.74±0.84	0.347	<0.05	1.000
MPV (fL)	9.58±0.61	9.92±0.67	9.92±0.62	0.292	<0.01	1.000

parameters following six months of DTG-based ART. Hemoglobin levels significantly increased post-treatment (from 11.13 ± 1.87 g/dL to 13.82 ± 1.55 g/dL, $p < 0.001$), although they remained significantly lower than in HIV-negative controls ($p < 0.001$), indicating partial reversal of HIV-related anemia. RBC count also rose markedly (from $4.28 \pm 0.47 \times 10^{12}/L$ to $4.78 \pm 0.52 \times 10^{12}/L$, $p < 0.001$), surpassing control levels ($p = 0.023$), signifying robust erythropoietic recovery. These findings support earlier reports demonstrating hematological benefits of ART, particularly with less myelotoxic agents like DTG [17–19], which may enhance erythropoietin response and suppress viral replication and hemolysis [20,21]. Red cell indices, including MCV, MCH, and MCHC, showed no significant changes; however, RDW-CV and RDW-SD decreased post-therapy, suggesting improved erythrocyte uniformity, albeit not significantly. Persistently elevated RDW values compared to controls may reflect residual inflammation, oxidative stress, or subclinical deficiencies [11]. Total WBC count increased in PLWH compared to controls ($p = 0.004$), aligning with Damtie *et al.* [22], though contrasting with Echefu *et al.* [23] and Talargia *et al.* [24]. In this study, lymphocyte percentage showed a significant decrease after six months of DTG-based ART. This reduction in lymphocyte percentage in the context of ART, may reflect a relative redistribution of immune cells rather than outright lymphopenia. These changes could also be indicative of resolution of relative increase in lymphocytes caused by uncontrolled viral replication and immune activation in untreated individuals [25]. The higher pre-treatment lymphocyte percentage observed in naïve individuals (46.37%) could have reflected immune hyperactivation or compensatory proliferation, which often diminishes after effective viral suppression. Neutrophil percentage rose significantly post-treatment ($p = 0.012$), indicating restored innate immunity, whereas absolute neutrophil counts declined significantly across both naïve and treated groups versus controls ($p < 0.05$), possibly due to environmental or co-infection factors [23,26]. Paired-sample analyses revealed no statistically significant changes in plateletcrit (PCT), platelet distribution width (PDW), mean platelet volume (MPV), or total platelet count (PLT) following initiation of DTG-based ART (all $p > 0.05$). These findings suggest that, over the short to medium term, DTG does not adversely impact platelet production, morphology, or activation. While descriptive trends indicated minor variations in PDW and MPV, these were not statistically or clinically significant. The hematologic neutrality observed aligns with existing evidence suggesting that DTG-containing regimens have a favorable safety profile with minimal hematotoxicity [4,7].

In conclusion, DTG-based ART appears hematologically safe with respect to platelet indices in this cohort. Future studies incorporating larger, age-matched populations and longer follow-up durations are warranted to further elucidate the long-term hematologic effects of INSTI-based

regimens. Age-related hematopoietic decline—particularly in erythroid and myeloid lineages—can affect hematologic parameters independently of HIV status or ART exposure. The age imbalance may partially account for some intergroup variations as known age-related physiological trends, and findings were stratified appropriately. Nonetheless, future studies will incorporate age-matched controls and larger cohorts to enhance external validity and minimize residual confounding. Despite these limitations, the study provides clinically relevant insight into the hematologic implications of DTG-based ART in a real-world sub-Saharan African cohort. Routine monitoring of full blood count parameters remains essential in PLWH, especially in resource-limited settings where advanced diagnostics are not readily accessible. Further longitudinal research is warranted to elucidate the long-term hematologic and metabolic consequences of INSTI-based regimens and to inform evidence-based treatment guidelines in diverse.

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