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Low burden of clinically relevant anaemia and thrombocytopenia among adolescents living with HIV receiving tenofovir/lamivudine plus dolutegravir: the CIPHER-ADOLA study in Cameroon

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Abstract

Background Anaemia and thrombocytopenia adversely affect adolescent HIV outcomes, yet adolescent-specific data from the tenofovir/lamivudine/dolutegravir (TLD) era remain scarce, and access to full blood count (FBC) testing is limited in Cameroon. We evaluated the prevalence, severity, and factors associated with these cytopenias among adolescents living with HIV (ADLHIV) in the TLD era.

Methods Multicentre cross-sectional study was conducted among ADLHIV (10–19 years) receiving TLD in the CIPHER-ADOLA cohort in Cameroon. Full blood count, viral load (VL) and CD4-count were performed. Factors associated with anaemia and thrombocytopenia were ascertained.

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Results A total of 252 ADLHIV was enrolled (50.8% male, 83.3% were vertically infected, and 7.2% were underweighted). ART-duration and TLD-exposure were 10 [6–13] years and 26 [12–33] months, respectively. Concerning virological response, 71.4%, 13.1%, and 15.5% had a VL < 50, 50–999, and ≥ 1000, respectively. Overall, 102 (40.5%) were anaemic, with only 2.9% severe. Anaemia rate was twice higher in females (55.6%, $p < 0.001$); 64.1% with VL ≥ 1000 against 35.0% with VL < 50 ($p = 0.003$); 60.0% with CD4 < 200 against 35.4% with CD4 > 500 ($p = 0.046$). Regarding thrombocytopenia, the burden was low (6.7%), but higher among VL ≥ 1000 ($p = 0.003$). Multivariate analyses showed a threefold higher anaemia prevalence in females (aOR [95% CI: 3.406 [1.8952-5.940]), fivefold without formal education (0.191 [0.047–0.776]), threefold in VL ≥ 1000 copies/ml (0.338 [0.156–0.733]). Thrombocytopenia was fourfold more likely in males (aOR: 0.236 [0.072–0.774]) and sevenfold more likely in individuals with VL ≥ 1000 copies/mL (aOR: 0.140 [0.038–0.510]).

Conclusion In the TLD era, anaemia remains common but generally mild, and thrombocytopenia is uncommon. Cytopenias were associated with unsuppressed viral load, with a stronger association for anaemia in females. These findings support programmatic targeted haemovigilance prioritising adolescents with unsuppressed viral load, particularly females, in settings where access to FBC testing is limited.

Keywords Adolescents living with HIV, Dolutegravir, Anaemia, Thrombocytopenia, Cameroon

Introduction

HIV infection remains a global public health threat, with approximately 40.8 million people living with HIV (PLWH) in 2024 [1]. Regarding paediatric populations, about 1.4 million children aged 0–14 years and 1.0 million adolescents aged 15–19 years were living with HIV in 2024 [1], with West and Central Africa (WCA) accounting for approximately 38% of new pediatric HIV infections globally [2]. In WCA, Cameroon has one of the highest HIV burdens among adolescents and young people. As of December 2022, approximately 29 789 children aged 0–14 years were living with HIV in Cameroon [3]. According to the National AIDS Control Committee (NACC), over 12 000 adolescents living with HIV (ADLHIV) aged 10–19 years were receiving combination antiretroviral therapy (cART) in Cameroon as of 2023 [4]. Despite improvements in treatment coverage, HIV-related morbidity and mortality remains unacceptably high among children and adolescents, partly due to persistent challenges in achieving and maintaining optimal viral suppression (VS) [5–7]. The recent adoption of dolutegravir-based regimens in Cameroon, using ABC/3TC/DTG for children under 30 kg and TDF/3TC/DTG (TLD) for those 30 kg or more, offers an opportunity to improve cART outcomes in this vulnerable population. Guidelines in Cameroon recommend monitoring viral load (VL) and CD4 count, with full blood counts (FBC) at baseline and as indicated to detect toxicity [8, 9]. However, in low- and middle-income countries (LMICs) like Cameroon, where co-endemic conditions affecting haematological outcomes are common, real-world data on haematologic outcomes and their predictors among adolescents on TLD are limited.

Anaemia and thrombocytopenia, two common haematological disorders, are widespread in LMICs among children and adolescents due to micronutrient deficiencies, endemic infections such malaria or enteric parasites and inherited haemoglobinopathies [10, 11]. Children and adolescents with HIV face additional threats from direct viral suppression of bone-marrow progenitors and chronic inflammation, as well as antiretroviral-related myelotoxicity, HIV-associated nutritional, and immunological vulnerabilities [10, 12–17]. Together, these factors substantially increase the burden of haematological complications in HIV-infected children and adolescents. Anaemia has long been recognized as an adverse effect of older cART regimens, most notably zidovudine; only minimal risk was observed with integrase strand transfer inhibitors (INSTIs) such as dolutegravir [18, 19]. cART-associated anaemia and thrombocytopenia might significantly worsen HIV-related mortality risk and impaired growth and neurocognitive development in children [20–23]. In addition, fatigue and other symptoms can undermine adherence and further complicate HIV management.

Despite the TLD's favourable haematological profile [21, 22], adolescent-specific programme data on anaemia and thrombocytopenia remain scarce, and most prior evidence are derived from adult cohorts or zidovudine-era regimens. Moreover, although full blood count (FBC) monitoring is recommended, it is not included in Cameroon's HIV programme free-test package and therefore requires out-of-pocket payment, limiting routine detection. In this context, real-world estimates of prevalence, severity, and associated factors; and risk strata that support targeted haemovigilance are needed to guide policy and optimise adolescent care on TLD. In a multicentre study in Cameroon, we aimed to estimate the prevalence and severity of anaemia and thrombocytopenia and to identify associated factors among adolescents living with HIV receiving TLD in Cameroon.

Materials and methods

Study design and population

A cross-sectional study with a multicentric approach was conducted among ADLHIV aged 10–19 years receiving TLD and enrolled within the frame of Collaborative Initiative for Paediatric HIV Education and Research (CIPHER) ADOLA study in the centre of Cameroon, which aimed to optimize the management of ADLHIV in Cameroon. All the 252 ADLHIV that were enrolled in the CIPHER-ADOLA cohort were included in this study.

Setting and description of the study sites

Four HIV/AIDS treatment centres with a large active file of ADLHIV including Chantal Biya Foundation, Essos Hospital Centre, Cité Verte District Hospital in urban areas, and Mbalmayo District Hospital in a rural area were selected for participants' enrolment. By incorporating different study locations and demographics, we aim to capture a more comprehensive understanding of the burden of anaemia and thrombocytopenia among adolescents receiving TLD in Cameroon. This multicentric approach provided insights into the challenges and opportunities in addressing ART driven anaemia and thrombocytopenia among adolescents on DTG-based ART. Laboratory investigations were carried out at the Chantal BIYA International Reference Centre for research on HIV/AIDS prevention and management (CIRCB, http://www.circb.cm/btc_circb/web).

The CIRCB is a reference public research institute of the Ministry of Public Health for the biological follow-up of PLHIV, including early diagnosis testing, viral load measurement, CD4 and CD8 T lymphocyte counts; biochemical and haematological tests and HIV resistance to antiretroviral drugs (HIVDR).

Participant enrolment and inclusion criteria

Adolescents living with HIV included in the 4 HIV/AIDS treatment centres were consecutively enrolled at their respective follow-up care units based on the following inclusion criteria: (a) aged 10–19 years living with HIV/AIDS, (b) starting or switching to the TDF/3TC/DTG protocol, (c) provided a signed parental authorisation and an assent for adolescents aged 12–19. Non-inclusion was based on : (a) presence of malaria parasite in thick blood film, and (b) inability to provide the required specimen or presence of intercurrent illness. Study information's sheet was provided to all participants and all the relevant written consent were obtained from parents/tutors and adolescents before enrolment. Participants were enrolled from December 2023 to January 2024.

Sample collection and processing

Briefly, 2 tubes of 4 mL of whole blood were collected in EDTA (Ethylenediamine tetra acetic acid) tubes by trained phlebotomists. Centrifugation of one tube was performed to obtain plasma which was then used to make two [2] aliquots of 1 ml each and stored at – 20 °C for viral load analysis using the Abbott m2000RT platform as per the manufacturer's instructions (http://www.abbottmolecular.com/products/infectious-diseases/realtime-pcr/hiv-1-assay). The second EDTA tube was used to perform the full blood count on the SYSMEX XN 1000 automated system and CD4 count analysis using CYFLOW PARTEC as per the manufacturer's instructions. The reliability and accuracy of the results were ensured by the systematic use of quality control panels.

Full blood count and blood smear

Full blood count was carried out using a SYSMEX XN 1000 automated haematological analyser according to the manufacturer's instructions (https://www.sysmex.com/US/en/products/hematology/xnseries/pages/xn-1000-hematology-analyzer.aspx). The system provides a complete blood count, involving a differential leucocyte count in 05 parts, a haemoglobin (Hb) concentration measurement, a quantitative platelet measurement, and determinant features of chromasia, microcytic and macrocytic anaemias. It also detects and flags parasitised red cells present in any blood sample under analysis. To roll out or confirm the presence of blood parasites, notably the malaria parasite, a thick blood smear was performed on all flagged samples. Additionally, blood smears were made and stained using the May Grunwald-Giemsa (MGG) stain to assess and record data on chromasia (staining intensity) and morphological differences (cell size and shape) detected by the haematological analyser.

CD4 count

The numeration of lymphocyte CD4 was processed on whole blood using CyFlow counter (Sysmex Corporation, Kobe, Japan) (https://www.wolflabs.co.uk/document/Sysmex-partec_flow-cytometers_cyflow-space_manual.pdf) by Flow Cytometry. According to the manufacturer's instructions, 20 µL of sample was mixed with a reagent (20 µL) containing CD4 mAb PE (monoclonal antibody phycoerythrin). These fluorochrome-labelled antibodies bind specifically to leukocyte surface antigens. The labelled samples are then treated with a buffer solution (800 µL) that lyses the red blood cells under mild hypotonic conditions while preserving the leukocytes through a light beam (green solid-state laser) at 532 nm. The data collected were analysed using CyView™ software and are presented in the form of histograms or graphs.

Quantification of plasma HIV-1 viral load

Quantification of HIV-1 viral load was performed on plasma samples using real-time Polymerase Chain Reaction (PCR) on the Abbott m2000rt HIV-1 platform

according to the manufacturer's instructions (http://www.abbottmolecular.com/products/infectious-diseases/realtime-pcr/hiv-1-assay). For RNA extraction, 0.6 mL of plasma was loaded into an Abbott m2000sp instrument, combined with the Abbott HIV-1 master mix containing an internal RNA control, primers, and probes targeting the pol-integrase gene. Amplification was performed using the Abbott m2000rt thermocycler after an initial sample preparation and automated extraction on the Abbott m2000sp instrument. The lower and higher detection limits were < 40 copies/mL and > 10,000,000 copies/mL HIV-1 RNA, respectively.

Variables and operational definitions

Sociodemographic (age, sex, rural/urban, education level) and clinical (BMI, ART duration, TLD duration, adherence, Viral, Hb, platelets, CD4) were collected. cART adherence was categorised according to the number of missed doses in the past 30 days based on self-report; good: ≥ 95% (1 day), moderate: 85–94% (2–4 days), and poor adherence: <85% (≥ 5 days) [24]. BMI was calculated and interpreted using sex-specific BMI-for-age percentiles; categorised as underweight (BMI less than the 5th percentile), normal (5th percentile to less than the 85th percentile), and overweight (85th percentile to less than the 95th percentile) [25]. Anaemia was defined as Haemoglobin (Hb) concentration < 12 g/dL, and categorized as mild (Hb 11–11.9 g/dL), moderate (Hb = 8–10.9 g/dL) and severe (Hb < 8 g/dL), according to WHO recommendations [26]. Thrombocytopenia was defined as a platelet count below 150×10^3 /mm^3, and categorized as mild (50,000–149,999 platelets/μL), moderate (20,000–49,999) and severe < 20,000 [26]. Viral suppression (VS) was defined as viral load (VL) < 1000 RNA copies/mL of plasma, and viraemia < 50 copies/mL was considered as the level of optimal viral control [27]. Finally, immune compromised individuals were defined as having a CD4 count < 500 cells/μL (moderate: 200–500 cells/μL, severe : < 200 cells/μL) [28].

Data collection, management and statistical analyses

Sociodemographic, clinical and treatment data were collected by trained investigators using standardized forms and structured questionnaire. All data were entered into a Microsoft Access database with restricted access. Quality control of data was ensured by double checking of data entry by a second investigator, and then validated by the supervisor. Quantitative and categorical variables were presented as median (interquartile range) and count (%), respectively. The medians were compared using Mann Whitney U test. Categorical variables were compared using Chi-square test or Fisher's exact test as appropriate. Multivariable logistic regression models were fitted for anaemia and thrombocytopenia. Candidate covariates (sex, age group, education level, BMI category, viral-load category, CD4 category, ART duration, TLD duration, setting) entered an initial model. We applied backward stepwise (conditional) elimination using the likelihood-ratio (LR) test, removing the least-contributory variable at each step (removal threshold $p > 0.10$). Calibration was assessed with the Hosmer–Lemeshow decile-of-risk test: participants were ordered by predicted probability and grouped into 10 risk deciles; $p \geq 0.05$ was interpreted as adequate calibration. Overall fit was summarised with McFadden's pseudo-R^2 (1 – log-likelihood(model)/log-likelihood(null)); values around 0.02–0.05 indicate small, ~ 0.10–0.20 moderate, and ≥ 0.20 strong improvement in fit. Multicollinearity was evaluated using variance inflation factors (VIFs) on the final design matrices (VIF < 5 low, 5–10 moderate, > 10 suggestive of problematic collinearity). Statistical significance was set at $p < 0.05$ and analyses were performed with IBM SPSS (version 20) and R.

Ethical considerations

This study adhered to all the principles outlined in the Helsinki Declaration, received ethical clearance from the Centre Region's Ethics Committee with reference: CE N° 0056 CRERSHC/2023 on March 14, 2023. Administrative approval was obtained from the regional delegation of public health for the Centre region, from the various data collection sites, and from CIRCB. A written parental authorization was obtained from all the participants; and adolescents aged 12–19 years provided a written assent. Anonymity was ensured throughout the study using only codes.

Results

Sociodemographic and clinical characteristics

Overall, 252 ADLHIV were analysed in this study, 50.8% were males. The median [IQR] age of the participants was 15 [13–17] years. About 76.6% had at least a secondary level education, while 4.8% (12/252) had no formal education. About 15.5% (39/252) lived in rural settings; 8.3% (21/252) and 8.7% (22/252) were respectively underweight and overweight (Table 1).

The median cART and TLD durations among ADLHIV were 10 [6–13] years and 26 [12–33] months, respectively. Notably, the median duration from seropositivity (diagnosis) was 7 [9–13] years. Concerning virological suppression, 71.4% (180/252) had achieved an optimal virological control (< 50 copies/mL), but 15.5% (39/252) were virally unsuppressed (viral load ≥ 1000 copies/mL). Regarding immunological response, about 28.2% (71/252) were immunocompromised [moderate: 26.2%, severe: 2.0% (5/252)]. Looking at Pre-TLD regimen exposition, a higher proportion of the ADLHIV enrolled

Table 1 Population characteristics and prevalence of anaemia among ADLHIV receiving TLD according to sociodemographic and treatment characteristics

Variables	Overall (*N* = 252)	Hb concentration < 12 g/dL (*N* = 102, 40.5%)	Hb concentration ≥ 12 g/dL (*N* = 150, 59.5%)	*p*-value
Sex, n (%)				
Males	128 (50.8)	33 (25.8)	95 (74.2)	**< 0.001**
Females	124 (49.2)	69 (55.6)	55 (44.4)	
Age group, n (%)				
10–14 years	121 (48.0)	52 (43.0)	69 (57.0)	0.437
15–19 years	131 (52.0)	50 (38.2)	81 (61.8)	
Setting, n (%)				
Rural	39 (15.5)	19 (48.7)	20 (51.3)	0.254
Urban	213 (84.5)	83 (39.0)	130 (61.0)	
Education level, n (%)				
No formal education	12 (4.8)	9 (75.0)	3 (25.0)	**0.030**
Primary	47 (18.6)	21 (44.7)	26 (55.3)	
Secondary/university	193 (76.6)	72 (37.3)	121 (62.7)	
Body mass index, n (%)				
Underweight	21 (8.3)	8 (38.1)	13 (61.9)	0.089
Normal	209 (82.9)	80 (38.3)	129 (61.7)	
Overweight	22 (8.7)	14 (63.6)	8 (36.4)	
ART adherence				
Good	181 (71.8)	74 (40.9)	107 (59.1)	0.964
Moderate	54 (21.4)	21 (38.9)	33 (61.1)	
Poor	17 (6.7)	7 (41.2)	10 (58.8)	
TLD duration in months, n (%)				
< 12	56 (22.2)	18 (32.1)	38 (67.9)	0.588
12–24	47 (18.7)	25 (53.2)	22 (46.8)	
> 24	124 (49.2)	48 (38.7)	76 (61.3)	
Unknown	25 (9.9)	11 (44.0)	14 (56.0)	
ART duration in years, n (%)				
< 5	39 (15.5)	22 (56.4)	17 (43.6)	0.181
5–10	98 (38.9)	36 (36.7)	62 (63.3)	
11–15	81 (32.1)	31 (38.3)	50 (61.7)	
> 15	34 (13.5)	13 (38.2)	21 (61.8)	
Pre -TLD regimen				
ABC/3TC/DTG	45 (17.9)	17 (37.8)	28 (62.2)	0.314
TDF/3TC/EFV (or ABC/3TC/EFV)	124 (49.2)	48 (38.7)	76 (61.3)	
ABC/3TC/LPV/r	28 (11.1)	13 (46.4)	15 (53.6)	
TDF/3TC/ATV/r	31 (12.3)	10 (32.3)	21 (67.7)	
Unreported	24 (9.5)	14 (58.3)	10 (41.7)	

P-values were computed using the fisher's exact or Pearson chi square tests as appropriate $p < 0.05$ was considered as statistically significant. *P*-values in bold indicate those with significant level

were on TDF/3TC/EFV, 49.2% (124/252) followed by ABC/3TC/DTG with 17.9% (45/252).

The prevalence of anaemia according to sociodemographic and treatment characteristics

The median [IQR] Hb-concentration was 12.2 [11.3–13.1] g/dL. Of the 252 ADLHIV, 40.5% were anaemic (< 12 g/dL). Anaemia rate was higher among females (55.6%), compared to males (25.8%, $p < 0.001$). We did not observe any significant difference according to duration on TLD and duration on ART.

Among the anaemic cases, 55.0% (56/102) had mild anaemia, 42.1% (43/102) had moderate anaemia, and only 2.9% (3/102) had severe anaemia. Figure 1 summarises the forms of anaemia based on severity. Microcytic hypochromic anaemia was the more frequent type observed among ADLHIV with moderate anaemia; and all individuals with severe anaemia experienced this type of anaemia. There was no reported case of malaria and/or infectious syndrome among the study participants. However, 1.2% (3/252) had flagged parasitised red blood cells but no malaria parasite was identified on thick blood smear.

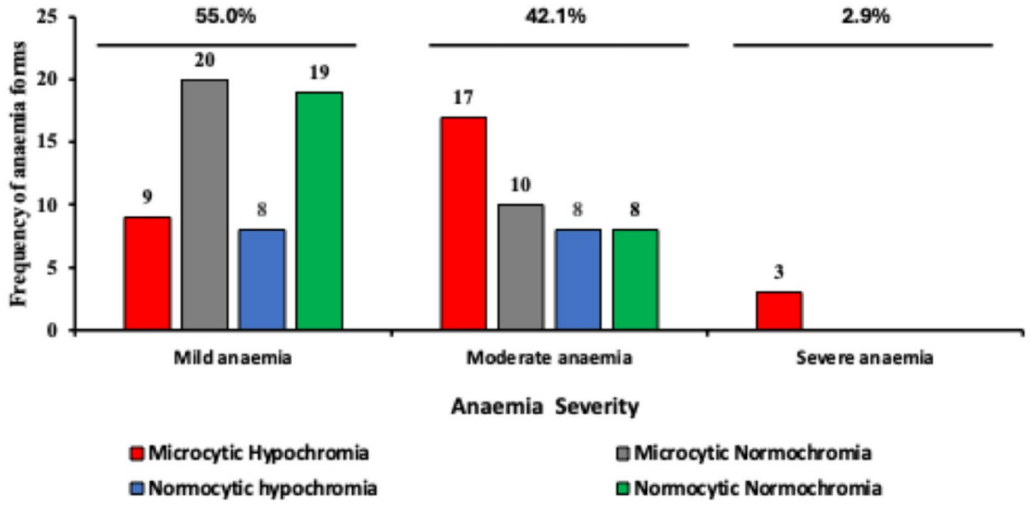

Fig. 1 Characteristic of different forms of anaemia among ADLHIV receiving TLD. Microcytic hypochromia was defined as MCV < 80 fL and MCHC < 32 g/dL; normocytic hypochromia defined as MCV (80–100fL) and MCHC < 32 g/dL; microcytic normochromia defined as MCV < 80 fL and MCHC (32–36 g/dL); and normocytic normochromia defined as MCV (80–100fL) and MCHC (32–36 g/dL) [29]

The prevalence of thrombocytopenia among ADLHIV receiving TLD according to sociodemographic and treatment characteristics

The rate of thrombocytopenia (thrombocyte count < 150,000 cells/mm^3) was low (6.7%) among ADLHIV receiving TLD, with only one case of severe thrombocytopenia. Table 2 summarises the prevalence of thrombocytopenia according to different sociodemographic and treatment characteristics. ADLHIV with < 5 years on ART had a significantly higher proportion of thrombocytopenia (15.4%) compared to those with longer duration, ($p = 0.036$).

Anaemia and thrombocytopenia rates according to viral load and CD4 count levels

The association between anaemia, thrombocytopenia, VL, and CD4 categories was summarized (Fig. 2). According to viral load, among virally unsuppressed ADLHIV, the proportion of anaemic individuals was significantly higher (64.1%), when compared to those with controlled viraemia (35.0%, $p = 0.003$), (Fig. 2A). Similarly, ADLHIV with lower CD4 values had higher thrombocytopenic rates. Notably, those with CD4 < 200cells/mm^3, had higher proportions of anaemic patients (60.0%), when compared to immunecompetent individuals (35.4%), ($p = 0.046$), (Fig. 2A). Compared to the non-anaemic group (709 [538–928] cells/mm^3), the anaemic-group had a significantly lower median CD4-count (592 [415–823], $p = 0.008$).

Concerning thrombocytopenia, individuals with controlled viraemia had a significantly lower frequency (3.3%), when compared to those with detectable viral load, ($p = 0.003$). Like in the case of anaemia, thrombocytopenia was significantly higher among immunocompromised individuals (Fig. 2B).

Anaemia and thrombocytopenia show a significant association with viral load. Anaemia and thrombocytopenia rates increased with an increase in VL, and were higher among virally non-suppressed ADLHIV, with 64.1% and 15.4%, respectively for anaemia and thrombocytopenia.

The double burden of anemia and thrombocytopenia in this study was 4.6% (11/252) and was fairly distributed among male (6/11) and female (5/11) ADLHIV enrolled.

Determinants of anaemia and thrombocytopenia among ADLHIV receiving TLD

At the multivariate level using the backward conditional regression model, gender, level of education, BMI, and VL were found to be independently associated with anaemia. Compared to males, females were about three times more likely to have anaemia (aOR [95% CI: 3.406 [1.8952–5.940]), (Table 3). ADLHIV with no formal education had about 5-times odds for anaemia compared to those with at least secondary/university level of education (aOR [95% CI: 0.191 [0.047–0.776]). Compared to ADLHIV with normal body weight, those overweight had 3-times odds for anaemia (aOR [95% CI: 0.328 [0.122–0.883]). ADLHIV with controlled viraemia were about 3-times less likely to develop anaemia compared to those experiencing virological non-suppression (aOR [95% CI: 0.338 [0.156–0.733]).

Backward conditional logistic regression (likelihood-ratio removal $p > 0.10$). Calibration assessed by the Hosmer–Lemeshow decile-of-risk test (10 groups); overall fit by McFadden's pseudo-R^2; multicollinearity screened with VIF. Anaemia model—HL χ^2=8.99 (df = 6), $p = 0.174$;

Table 2 The prevalence of thrombocytopenia among ADLHIV receiving TLD

Variables	Overall (*N* = 252)	Thrombocytes count < 150 000 cells/mm^3 (*N* = 17, 6.7%)	Thrombocytes count ≥ 150 000 Cells/mm^3 (*N* = 235, 93.3%)	*p*-value
Sex, n (%)				
Males	128 (50.8)	12 (9.4)	116 (90.6)	0.091
Females	124 (49.2)	5 (4.0)	119 (96.0)	
Age groups, n (%)				
10–14 years	121 (48.0)	8 (6.6)	113 (93.4)	0.935
15–19 years	131 (52.0)	9 (6.9)	122 (93.1)	
Setting, n (%)				
Rural	39 (15.5)	4 (10.3)	35 (89.7)	0.310
Urban	213 (84.5)	13 (6.1)	200 (93.9)	
Level of education, n (%)				
No formal education	12 (47.8)	2 (16.7)	10 (83.3)	0.198
Primary	47 (18.6)	4 (8.5)	43 (91.5)	
Secondary/university	193 (76.6)	11 (5.7)	182 (94.3)	
Body mass index, n (%)				
Underweight	21 (8.3)	1 (4.8)	20 (95.2)	0.351
Normal	209 (82.9)	13 (6.2)	196 (93.8)	
Overweight	22 (8.7)	3 (13.6)	19 (86.4)	
ART adherence				
Good	181(71.8)	13 (7.2)	168 (92.8)	1.000
Moderate	54 (21.4)	3 (5.6)	51 (94.4)	
Poor	17 (6.7)	1 (5.9)	16 (94.1)	
TLD duration in months, n (%)				
< 12	56 (22.2)	3 (5.4)	53 (94.6)	1.000
12–24	47 (18.7)	4 (8.5)	43 (91.5)	
> 24	124 (49.2)	9 (7.3)	115 (92.7)	
Unknown	25 (9.9)	1 (4.0)	24 (96.0)	
ART duration in years, n (%)				**0.005**
< 5	39 (15.5)	6 (15.4)	33 (84.6)	
5–10	98 (38.9)	8 (8.2)	90 (91.8)	
11–15	81 (32.1)	3 (3.7)	78 (96.3)	
> 15	34 (13.5)	0 (0.0)	34 (100.0)	
Pre-TLD regimen				
ABC/3TC/DTG	45 (17.9)	4 (8.9)	41 (91.1)	0.429
TDF/3TC/EFV(or ABC/3TC/EFV)	124 (49.2)	6 (4.8)	118 (95.2)	
ABC/3TC/LPV/r	28 (11.1)	4 (14.3)	24 (85.7)	
TDF/3TC/ATV/r	31 (12.3)	2 (6.5)	29 (93.5)	
Unreported	24 (9.5)	1 (4.2)	23(95.8)	

P-values were computed using the fisher's exact or Chi square tests as appropriate, $p < 0.05$ was considered statistically significant. P-values in bold indicate those with significant level

McFadden's pseudo-R^2=0.128; maximum VIF = 7.75. Thrombocytopenia model (reduced specification)—HL χ^2=4.42 (df = 5), $p = 0.490$; McFadden's pseudo-R^2=0.192; maximum VIF = 3.70. Bold p-values indicate statistical significance at $\alpha = 0.05$.

For thrombocytopenia, gender, ART duration and viral load were found to be independently associated factors. Compared to females, males were 4-times more likely to have thrombocytopenia (aOR [95% CI: 0.236 [0.072–0.774]). ADLHIV who have been on cART for 11–15 years had about 5-times lesser odds of experiencing thrombocytopenia, compared to those on ART for less than five years (aOR [95% CI: 0.178 [0.036–0.825]). Compared to ADLHIV with controlled viremia (< 50 copies/mL), those with failure (VL ≥ 1000 copies/mL) were 7-times more likely to have thrombocytopenia (aOR [95% CI: 0.140 [0.038–0.510]), (Table 3).

Discussion

This study was a cross-sectional study with a multicentric approach conducted among 252 ADLHIV aged 10–19 years receiving TLD in Cameroon. We showed

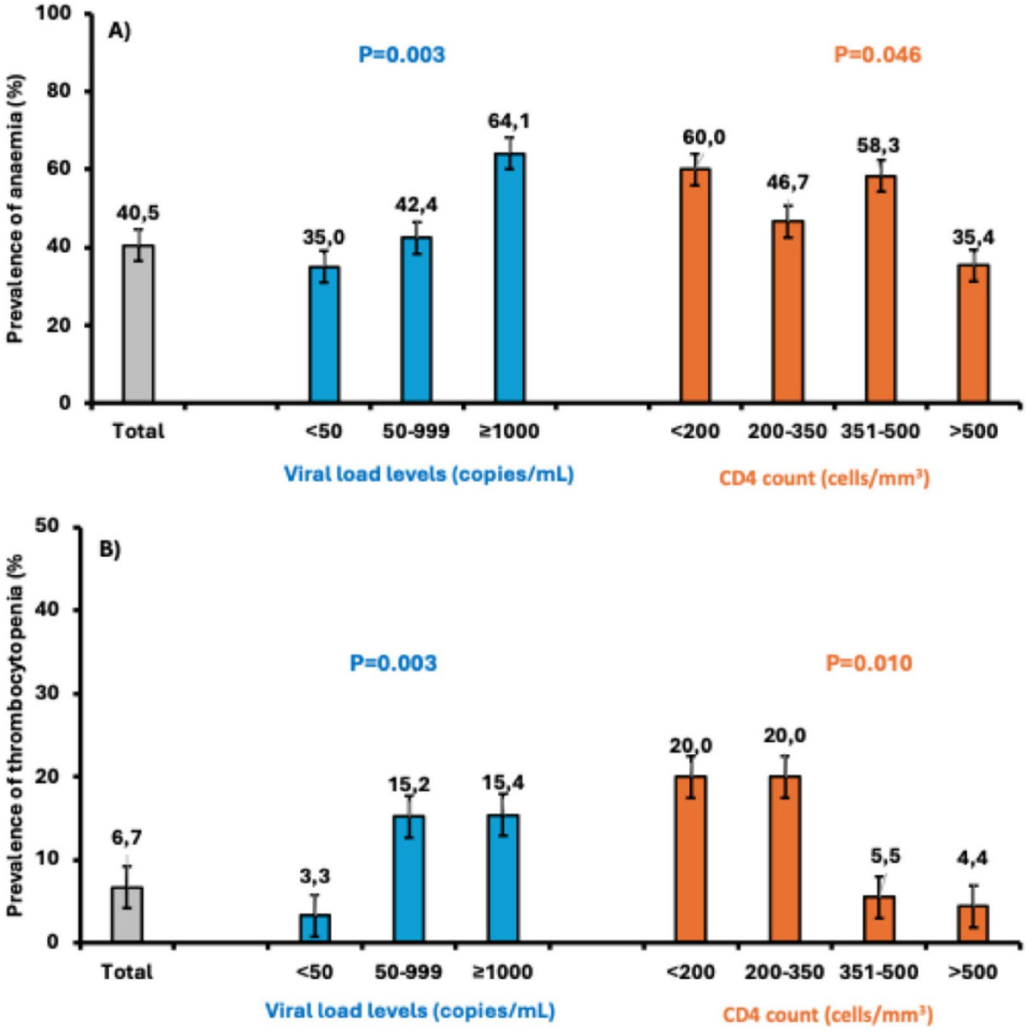

Fig. 2 Anaemia and thrombocytopenia rates according to viral load and CD4 count level. **A** Platelets count < 150,000 cells/mm^3 **B** Hemoglobin concentration < 12 g/dL

that more than 40% of the ADLHIV on TLD were anaemic, with 42.1% and 2.9% having respectively a moderate and severe forms of anaemia. Among these anaemic adolescents, microcytic hypochromia and microcytic normochromia were frequent, depicting a moderate but quite concerning condition. This result is partly consistent with a previous finding where it was observed that microcytic hypochromia and normocytic normochromia were more predominant [30], however, different data exist on this aspect [31]. Although mild to moderate anaemia was more prevalent, the high proportion of ADLHIV affected underscores the need for tailored interventions targeting the monitoring of hematological profile among children and adolescents living with HIV. A cohort study of 119 patients conducted in the Democratic Republic of Congo in the era of DTG noted that 21.0% of patients presented with some forms of anaemia at the start of DTG [32]. Some studies reported as high as 66% of anaemia rate after treatment initiation [33]. A study in Ethiopia showed that upon DTG-based regimen administration, the burden of anaemia reduced by 50.0% [34]. In developing countries, a systematic review on the prevalence of anaemia among PLHIV in 2022 reported a prevalence of 46.6% among people aged ≥ 15 [35]. Our results is in line with some of these reports and highlight the burden of haematological disorders that deserve an attention, even in the new era of modern ART [33]. Although there are disparities in findings across studies, the generally high burden of anaemia reported highlights the complexity of haematological responses in HIV treatment across different settings in sub Sahara Africa (SSA). Black people and young children are more prone to anemia due to both constitutional and social/geographical factors [36–41]. The endemicity of malaria, nutritional deficiencies, typical blood disorders such as carriers of S mutation, and other tropical conditions common in SSA significantly contribute to the overall anaemia burden [42, 43]. Conversely, the prevalence of thrombocytopenia

Table 3 Factors associated with anaemia and thrombocytopenia in ADLHIV receiving TLD

Variables	Multivariate regression model	
	aOR (95% CI)	*P*–value
Anaemia		
Gender		
Male	1	
Female	3.406 (1.952–5.940)	**< 0.001**
Level of education		
No formal education	1	
Primary	0.292 (0.065–1.302)	0.106
Secondary/university	0.191 (0.047–0.776)	**0.021**
Body mass index level		
Underweight	0.326 (0.083–1.277)	0.108
Normal weight	0.328 (0.122–0.883)	**0.027**
Overweight	1	
Viral load (copies/mL)		
< 50	0.338 (0.156–0.733)	**0.006**
50–999	0.369 (0.132–1.031)	0.057
≥ 1000	1	
Thrombocytopenia		
Gender		
Male	1	
Female	0.236 (0.072–0.774)	**0.017**
ART duration (years)		
< 5	1	
5–10	0.447 (0.131–1.524)	0.198
11–15	0.178 (0.038–0.825)	**0.027**
> 15	–	0.998
Viral load (copies/mL)		
< 50	0.140 (0.038–0.510)	**0.003**
50–999	0.812 (0.204–3.231)	0.768
≥ 1000	**1**	
CD4 (cells/mm^3)		
< 200	20.974 (0.435-1012.396)	0.124
200–350	4.023 (0.707–22.900)	0.117
350–500	0.747 (0.120–4.641)	0.754
> 500	1	

was low (6.7%), with only one ADLHIV presenting with severe thrombocytopenia (< 50 cells/mm^3). Reports from other studies have indicated considerably higher (up to 20%) thrombocytopenia rates [33, 44]. In the same light, a previous study in Cameroon conducted prior to the introduction of TLD as the preferred first line treatment reported a similar rate of thrombocytopenia (6.9%) among ART-treated patients [45].

Our study shows that the burden of anaemia and thrombocytopenia were associated with ongoing viral replication. Anaemia and thrombocytopenia rates were respectively 3 times and 7 times higher in virally non-suppressed ADLHIV, when compared to those with controlled viremia (Table 3). However, because this analysis is cross-sectional, based on a single VL measurement at enrolment, these findings should be interpreted as associations rather than causal effects. Virological non-suppression may also reflect unmeasured factors, including baseline resistance and social/structural constraints. TLD based regimens have shown remarkable improvement in achieving virological suppression (VS) targets across many countries [46, 47]. It is well documented that ongoing HIV replication induces inflammation and immune activation, leading to cytokine-mediated suppression of haematopoietic progenitor cell proliferation and differentiation [48, 49]. This finding aligns with report by Marchionatti et al., who showed that the prevalence of thrombocytopenia and anaemia were worsened by increased viral load, co-infections or opportunistic infections [10]. This underscores the importance of achieving and maintaining the third 95% UNAIDS target [50] in order to improve the heath outcomes in this fragile population.

As expected, anaemia rate in this study was higher in females, with three times higher odds of becoming anaemic compared to males. This report is consistent with findings from other studies that identified sex as a determinant of anaemia in HIV-infected populations. Combination of biological factors, including menstrual blood loss, hormonal influences, hepcidin-mediated iron regulation, genetic predisposition, and nutritional status predisposes adolescent females to anaemia. Menstruation leads to regular blood loss and higher iron requirements, while hormonal fluctuations across the menstrual cycle can affect iron metabolism and absorption. Hepcidin, a key regulator of iron homeostasis, increases with inflammation and certain hormonal signals, restricting intestinal absorption and iron release from stores. In adolescents, sex- and gender-related social and nutritional constraints, including food insecurity, low dietary diversity, limited access to iron/folate, and barriers to menstrual health may compound biological risk for anaemia; these factors were not measured in this study [14, 51–53].

Regarding thrombocytopenia, male sex was independently associated with experiencing anaemia. Furthermore, ART duration and viral load were identified as critical determinants of thrombocytopenia, highlighting the importance of tailored treatment strategies and regular monitoring to mitigate risks associated with long-term ART.

Currently, it should be noted that in Cameroon, FBC is not part of the package provided free of charge (user fees) to support the follow-up of PLHIV. This limits their access, especially the pediatric population who might have higher risk of other diseases such as malaria. Facilitating the access of ADLHIV who has been shown to experience a considerable burden of anaemia even in the presence of modern cART such as TLD should be prioritized.

A main limitation of this study is the lack of universal thick-film screening; thick blood smears were not performed for all participants, so subclinical parasitaemia may have been missed. The study is cross-sectional, relies on a single viral-load measurement at enrolment, and has no comparator regimen; findings are therefore associative, regimen-attributable effects cannot be estimated, and unmeasured confounding is possible. Given the high prevalence of haemoglobin S in Cameroon, future studies should include haemoglobin S screening to distinguish genetic causes from non-genetic anaemia. Despite these limitations, our multivariable analyses identified factors associated with anaemia and thrombocytopenia; notably, unsuppressed viral load was associated with cytopenias and serves as an operational criterion for prioritising haemovigilance.

Conclusions

In the TLD era, anaemia remains common but generally mild, while thrombocytopenia is uncommon among ADLHIV. Anaemia was associated with unsuppressed VL, particularly in females and in those with no formal education, whereas thrombocytopenia was associated with male sex, shorter ART duration, and unsuppressed VL. These findings support programmatic targeted haemovigilance that prioritises ADLHIV with unsuppressed VL, particularly females, in LMIC settings where access to FBC testing is limited.

Abbreviations

ADLHIV	Adolescents living with HIV
BMI	Body Mass Index
cART	Combination antiretroviral therapy
CD4	Cluster of differentiation 4
CD8	Cluster of differentiation 8
CIRCB	Chantal BIYA International Reference Centre for research on HIV/AIDS prevention and management
EDTA	Ethylenediamine tetra acetic acid
Hb	haemoglobin
HIV	Human Immunodeficiency Virus
IL-6	Interleukin-six
IL-1β	Interleukin one-beta
INSTI	Integrase strand transfer inhibitor
LMICs	Low- and middle-income countries
mAb PE	Monoclonal antibody phycoerythrin
MCV	Mean corpuscular volume
MGG	May Grunwald-Giemsa
NACC	National AIDS Control Committee
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NRTI	Nucleoside reverse transcriptase inhibitor
PCR	Polymerase Chain Reaction
PLHIV	People living with HIV
PWH	People with HIV
TLD	Tenofovir/lamivudine/dolutegravir
TNF-α	Tumor necrosis factor-alpha
UNAIDS	Joint United Nations Programme on HIV/AIDS
VL	Viral load
VS	Virological suppression
WCA	West and Central Africa
ZDV	Zidovudine

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Author contributions

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Data availability

Data are available upon request from the corresponding authors.

Declarations

Ethics approval and consent to participate

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the ethics committee of the regional delegation of public health for the Centre region of Cameroon (CE No 0056 CRERSHC/2023) on 14 March 2023.

Competing interests

The authors declare no competing interests.

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