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Original Research Article

Haematological profile of HIV positive adults co-infected with pulmonary tuberculosis: a nested cross-sectional study in Uganda

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ABSTRACT

Background: Tuberculosis an endemic disease in Uganda contributes to over 30% of deaths among people living with HIV (PLHIV). Challenges in early diagnosis and monitoring common in limited resource settings underscore the need for more cost effective and reliable methods to improve patient outcomes. Hematological parameters have emerged as potential markers for predicting and monitoring TB disease. This study aimed to evaluate the hematological parameters among HIV/TB co-infected patients enrolled from both outpatient and inpatient health facility settings in Uganda.
Methods: A nested cross-sectional study involving 120 participants (active-TB-40; latent-TB-25; no-TB-55) was conducted from June 2024 to May 2025 at Kisenyi HCIV (outpatient) and Kiruddu Hospital (inpatient) in Uganda. Venous blood was collected in ethylene diamine tetra acetic (EDTA) tubes and analyzed using flow cytometry technique. C-reactive protein (CRP) was measured using the immunoturbidimetry and nephelometry method. Data obtained was analyzed using Stata version 23.
Results: The active-TB group showed lower red blood count, hemoglobin, hematocrit, mean cell hemoglobin and mean cell volume compared to the latent-TB and no-TB groups (p=0.001). CRP was significantly higher in the active TB group (p=0.001). The active-TB group had high total WBC count (p=0.02) with increased neutrophil count (p=0.003). No significant differences were observed in lymphocyte counts across the 3 patient groups (p=0.217).
Conclusions: Hematological parameters provide a reliable tool for risk profiling and monitoring among PLHIV coinfected with TB especially in resource limited settings. Therefore, integrating these parameters in routine care and management for TB/HIV patients may improve patient outcomes.

Keywords: Anemia, Hematological parameters, HIV, TB/HIV coinfection, Tuberculosis

INTRODUCTION

Tuberculosis (TB), caused by *Mycobatectrium tuberculosis* (MTB) remains the leading cause of mortality among people living with HIV (PLHIV) globally accounting for up to 13% of AIDs related deaths.[1] Uganda, a country categorised as endemic to TB has an estimated incidence rate of 200 cases per 100,000 population, and about 40% of PLHIV are co-infected with TB.[2,3] In 2022, upto 30% of deaths among PLHIV in Uganda were attributed to TB.[2]

Among PLHIV whose immune competencies are already compromised, co-infection with TB a disease known for

its chronicity and systemic involvement creates double trouble in diagnosis, care and management. The clinical presentation and progression of tuberculosis is influenced by the host's innate and adaptive immune responses. This involves the phagocytic attack of the inhaled antigen (MTB) by macrophages (neutrophils and dendritic cells) and subsequently activating T-cell immunity through the release of cytokines through a complex immune reaction.[4,5]

Tuberculosis, a multi-systemic disease can affect the bone marrow leading to subsequent hematological abnormalities that influence the host's inflammatory response and consequently disease progression.[6,7] Abnormalities in the hematological parameters among TB patients are common, with deviations in red blood cell (RBC) count, hemoglobin concentration, hematocrit, and other parameters frequently reported.[8-10] These abnormalities often reflect the systemic impact of the disease and have potential to be used by clinicians to assess disease progression, treatment response, and overall prognosis in TB patients.[11,12]

In the context of HIV and TB co-infection, the clinical utility of hematological parameters lies in their simple and cost effective valuable adjunct to existing diagnostic methods, particularly in limited resource settings where access to advanced diagnostic methods maybe unavailable.[9,13] For example, anemia among TB patients has been attributed to the suppression of erythropoiesis due to bone marrow infiltration coupled with nutritional deficiencies secondary to the chronic state of the illness.[14,15]

Previous studies have highlighted prevalence rates of anemia among TB patients from 31% to as high as 77%, depending on factors like coinfection status, nutritional status and disease severity.[9,16] In addition, studies have reported the observed leukocytosis and neutrophilia among TB infected patients to be as a result of the body's attempt to mount an effective immune response against the invading pathogen.[17-19] A cross-sectional study among TB patients in Kenya reported a 15.9% prevalence rate of raised white blood cell (WBC) count.[8]

These observations underscore the value of hematological assessments as a viable tool to enhance risk stratification, treatment outcome, and targeted interventions among HIV/TB co-infected patients, especially in endemic settings like Uganda.

Aim of the study

Our study aimed to evaluate the hematological parameters among HIV/TB co-infected patients enrolled from both outpatient and inpatient health facility settings in Uganda. Findings for which could potentially enhance clinical decision-making and improve patient management and outcomes within this demography.

METHODS

Study site

The study was conducted at Kisenyi Health Centre IV and Kiruddu National Referral Hospital both located in Kampala- Uganda from June 2024 to May 2025. Kisenyi HCIV provided patients from an outpatient setting while Kiruddu provided inpatients.

Study design

A cross-sectional study nested within a prospective cohort involved HIV positive patients attending the outpatient clinic at Kisenyi HCIV and those admitted at Kiruddu National Referral Hospital (NRH).

Study population

The study involved HIV positive patients attending Kisenyi antiretroviral treatment (ART) clinic and those admitted at Kiruddu NRH and were categorised into 3 groups i.e., active-TB, latent TB and no-TB. The active-TB patients were those who had a microbiological diagnosis of TB at enrolment (positive GeneXpert or sputum culture test). The latent- TB group were those who at enrolment had no clinical signs and symptoms of TB and had a positive interferon gamma release assay (IGRA) test result. The no-TB group were those without any clinical signs and symptoms of TB and their IGRA test result was negative.

Sample size

Yamane's (1967) formula for sample size calculation was used to calculate the required study sample size.

$n=N/1+N(e^2)$

Where; n is the sample size, N=215 is the average monthly number of TB patients seen at both Kisenyi HCIV and Kiruddu NRH, and e is the margin of error (or desired level of precision) set at 95% confidence level. The sample size was calculated as follows: n=215/1+215 (0.05)2≈ 139.8 ≈ 140 patients.

Sampling technique

Patients with microbiologically confirmed TB were recruited from the TB clinic at Kisenyi HCIV or from the pulmunology ward at Kiruddu NRH. The HIV positive clients coming in for routine ART refill and without any clinical signs and symptoms of TB that voluntarily consented to take part in the study were recruited in the latent TB group if they turned out with a positive IGRA test or stratified in the no-TB group if their IGRA test was negative. All study participants were recruited based on the eligibility criteria and this allowed for a comprehensive analysis of the hematological profile

among the patients and facilitated the comparison of results between the three groups.

Inclusion criteria

Patients were included in the study if they were adults (≥18 years) of known HIV positive status and had a microbiological evidence of TB diseases (positive GeneXpert or mycobacterial culture) for the active TB group; had no clinical signs and symptoms of TB with a positive IGRA test for latent-TB group and for the no-TB group, they had no clinical signs and symptoms of TB and their IGRA test results were negative.

Exclusion criteria

Participants were excluded from the study if at the time of enrolment, the follow-up visit was judged to be poorly feasible (e.g., individuals planning to relocate) or those participants who had conditions or circumstances that preclude their participation based on the judgement of the site investigator.

Anthropometric measurements

Participants' weight was taken using a standard calibrated SEKA-brand weighing scale and weight was recorded in kilograms (kg). The height was measured using a calibrated height meter scale mounted on the wall and recorded in meters. The participant's body mass index (BMI) was then calculated using the formula below;

$$BMI = \text{weight (kg)} / \text{height (m)}^2$$

The participants' mid-upper arm circumference (MUAC) was measured using a standard calibrated MUAC tape and recorded in centimeters (cm) while the biceps skin fold was measured using a calibrated venire caliper and documented in millimeters (mm).

Sample collection

Sample collection from participants was performed by a trained study nurse or medical doctor following the study clinical manual of procedures (MOP). Eligible participants underwent preparation for venous blood sample collection including counselling on potential risks. A gauge 21 butterfly needle was inserted into the anterior cubital fossa vein and whole blood was collected for each of the patients directly into a 4 ml ethylene diamine tetra acetic (EDTA) BD-vacutainer that was correctly labeled with the patient's identification number.

Blood samples processing and analysis

Venous blood samples collected in EDTA BD-vacutainer tubes were analyzed using the Mindray BC760 cell counter, which utilized flow cytometry. This tested for total white blood cell, total red blood count, differential count for neutrophils, lymphocytes, monocytes, basophils and platelets. The procedure involved mixing the blood sample with the anticoagulant in the tube, and utilizing internal and external controls for quality assurance. The CD4 count test was analysed using BDFACSPRESTO™ V01.00.02.5580C machine which utilizes flow cytometry. C-reactive protein (CRP) was measured using the immunoturbidimetry and nephelometry method.

Data analysis

The data obtained was analyzed using Stata version 23 to obtain the mean and p values for the independent samples t-test. The independent samples t-test was used to determine if there was a statistically significant variation in the hematological profiles between the three groups. The results were presented in tables and figures.

RESULTS

Clinical-social characteristics of the study participants

The study comprised 120 participants (i.e., active TB- 40, latent TB- 25 and No TB- 55), with majority being males (68; 56.7%). The median age was 36 years (30,43). More than two-thirds (73.3%) of the participants were on antiretroviral treatment (ART) and the average duration on ART was 5.8 years (SD=5.0). Within the active TB group, the most prevalent symptoms were cough (97.5%), unintended weight loss (87.5%), night sweats and fevers both at 67.5% (Table 1).

Anthropometric characteristics of the study participants

The average body mass index (BMI) of the study participants was 21.9 ($p<0.001$), with majority (71; 59.2%) having normal BMI. However, the active-TB group had the highest number of patients (16/40; 40%) in the underweight category compared with the no-TB (6/55; 10.9%) and latent-TB (3/25; 12%) groups. The average mid-upper arm circumference (MUAC) was 25.0 cm, but lowest in the active TB group (22.9 cm). The average biceps skin fold was 8.2 mm and was thinnest among the active TB group (7.6 mm) (Table 2).

Hematological and immunological parameters of the study participants

Immunological parameters

The mean±SD of study participants' c-reactive proteins (CRP) was 33.7±54.8 and was highest (79.1±65.5) among the active TB group and lowest in the latent-TB (5.3±9.3) group. The active-TB group had the majority patients (34/40; 85%) with recorded high CRP levels compared with latent-TB (3/25; 12%) and No-TB (13/55; 23.6%) groups. The mean±SD of participants' CD4 count was 450±349.3 and was highest in the latent-TB group (691.8±265.2) and lowest in the active TB group (229.0±245.8) (Table 3).

Table 1: Clinical-social characteristics of the study participants.

Variables	Total participants	No TB	Active TB	Latent TB
N (%)	120 (100)	55 (45.8)	40 (33.3)	25 (20.9)
Sex				
Male N (%)	68 (56.7)	25 (45.5)	30 (75)	14 (56)
Female N (%)	52 (43.3)	30 (54.5)	10 (25)	11 (44)
Median age- years (Q1, Q3)	36 (30, 43)	35 (28, 43)	35 (30.25, 39)	43 (32.75, 45)
ART status				
Yes N (%)	88 (73.3)	43 (78.2)	20 (50)	25 (100)
No N (%)	32 (26.7)	12 (21.8)	20 (50)	0 (0)
Average duration on ART in years (SD)	5.8 (5.0)	5.9 (5.0)	4.0 (3.8)	7.1 (5.7)
Clinical symptoms				
Cough- N (%)	41 (34.2)	2 (3.6)	39 (97.5)	0 (0.0)
Night sweats- N (%)	27 (22.5)	0 (0.0)	27 (67.5)	0 (0.0)
Unintended Weight loss- N (%)	39 (32.5)	4 (7.3)	35 (87.5)	0 (0.0)
Fevers- N (%)	32 (26.7)	5 (9.1)	27 (67.5)	0 (0.0)
Hemoptysis- N (%)	3 (2.5)	0 (0.0)	3 (7.5)	0 (0.0)
Chest pain- N (%)	6 (5.0)	0 (0.0)	6 (15)	0 (0.0)
Fatigue- N (%)	6 (5.0)	3 (5.5)	3 (7.5)	0 (0.0)
Loss of appetite	10 (8.3)	5 (9.1)	4 (10.0)	1 (4.0)

Table 2: Anthropometric characteristics of the study participants.

Variable	Total participants	No TB	Active TB	Latent TB	P value
Body Mass Index (BMI), mean (SD)	21.9 (4.0)	23.1 (4.0)	19.7 (2.8)	22.9 (4.3)	<0.001
MUAC- cm, mean (SD)	25.0 (3.6)	26.1 (3.5)	22.9 (2.7)	26.2 (3.6)	<0.001
Biceps skin fold- mm, mean (SD)	8.2 (6.4)	8.1 (6.2)	7.6 (5.4)	9.1 (8.0)	0.669

Table 3: Hematological and immunological parameters of the study participants.

Variables	Total participants	No TB	Active TB	Latent TB	P value
Immunological parameters					
CRP mean (SD)	33.7 (54.8)	13.7 (34.0)	79.1 (65.5)	5.3 (9.3)	<0.001
CD4 count mean (SD)	450 (349.3)	486.4 (355.0)	229.0 (245.8)	691.8 (265.2)	<0.001
Hematological parameters					
Hemoglobin- (gm/dl) mean (SD)	13.0 (2.5)	13.6 (2.3)	11.3 (2.1)	14.4 (2.0)	<0.001
HCT (%) mean (SD)	41.9 (7.8)	43.7 (7.4)	36.7 (6.4)	46.1 (5.9)	<0.001
MCV- (fL) mean (SD)	92.7 (11.4)	93.1 (11.0)	89.2 (12.1)	97.6 (9.3)	0.018
MCH- (pg) mean (SD)	29.0 (3.6)	29.3 (3.0)	26.6 (4.1)	30.4 (3.4)	0.007
MCHC- (gm/dl) mean (SD)	310.9 (12.5)	311.9 (13.3)	309.0 (12.6)	311.5 (9.6)	0.534
RBC count- ($x10^{12}$/l) mean (SD)	4.5 (0.8)	4.7 (0.8)	4.2 (0.7)	4.7 (0.6)	0.001
RDW-cv (%) mean (SD)	14.1 (2.8)	13.4 (2.5)	15.5 (3.2)	13.3 (1.3)	<0.001
WBC count- ($x10^9$/l) mean (SD)	4.9 (2.9)	4.4 (1.5)	5.9 (4.4)	4.3 (1.4)	0.020
Neut count- ($x10^9$/l) mean (SD)	2.8 (2.7)	2.3 (1.4)	3.9 (4.0)	1.9 (1.1)	0.003
Lymp count- ($x10^9$/l) mean (SD)	7.8 (54.4)	1.5 (0.6)	20.2 (93.4)	1.9 (0.5)	0.217
Plt count- ($x10^9$/l) mean (SD)	255.5 (101.7)	243.6 (79.4)	279.0 (131.7)	244.7 (82.8)	0.224

White blood cell parameters

The mean±SD of the total white blood cell count for study participants was within normal ranges i.e., 4.9±2.9x10^9/l (p=0.020). However, the latent-TB group had the majority of patients (14/25; 56%) with the mean WBC categorized as leukopenia (<4.0x10^9/l) while the active-TB group had majority patients (5/40; 12.5%) with leukocytosis (>11.0x10^9/l). The absolute neutrophil count (mean±SD) of the study participants was normal at 2.8±2.7x10^9/l (p=0.003), but lowest among the latent-TB group (1.9±1.1x10^9/l) with 17 out of 25 (68%) patients categorized as having neutrophilia in this group compared with the active-TB (11/40; 27.5%) and no-TB (28/55; 50.9%). There was noted lymphopenia among 16 out of

40 (37.5%) patients with active-TB at 1.2±0.86x10^9/l (Table 3).

Red blood cell parameters

The absolute (mean±SD) red blood cell count (RBC) of the study participants was within normal range of 4.5±0.8x10^{12}/l (p=0.001), with generally no difference across the no-TB (4.7±0.8x10^{12}/l), latent-TB (4.7±0.6x10^{12}/l) and active TB (4.2±0.7x10^{12}/l) groups. The mean corpuscular hemoglobin concentration (MCHC) of the study participants was generally normal at 29.0±3.6 pg (p=0.007). However, the MCH level among the active-TB group was below the normal range (26.6±4.1 pg) compared to the no-TB (29.3±3.0 pg) and latent-TB (30.4±3.4 pg) groups. Similarly, MCHC of the study participants was normal at 31.1±12.5 gn/dl (p=0.534) and no significant difference across the three groups; i.e., No-TB (31.2±13.3 gm/dl), latent-TB (31.2±9.6 gm/dl) and active-TB (30.9±12.6 gm/dl). The mean corpuscular volume (MCV) of the study participants was normal at 92.7±11.4 fl (p=0.018) with no significant differences across the no-TB (93.1±11.0 fl), latent-TB (97.6±9.3 fl) and active-TB (89.2±12.1 fl) groups (Table 3). The majority of patients classified as anemic under the active-TB group had a microcytic (10/40; 25%), hypochromic (17/40, 42.5%) type of anemia.

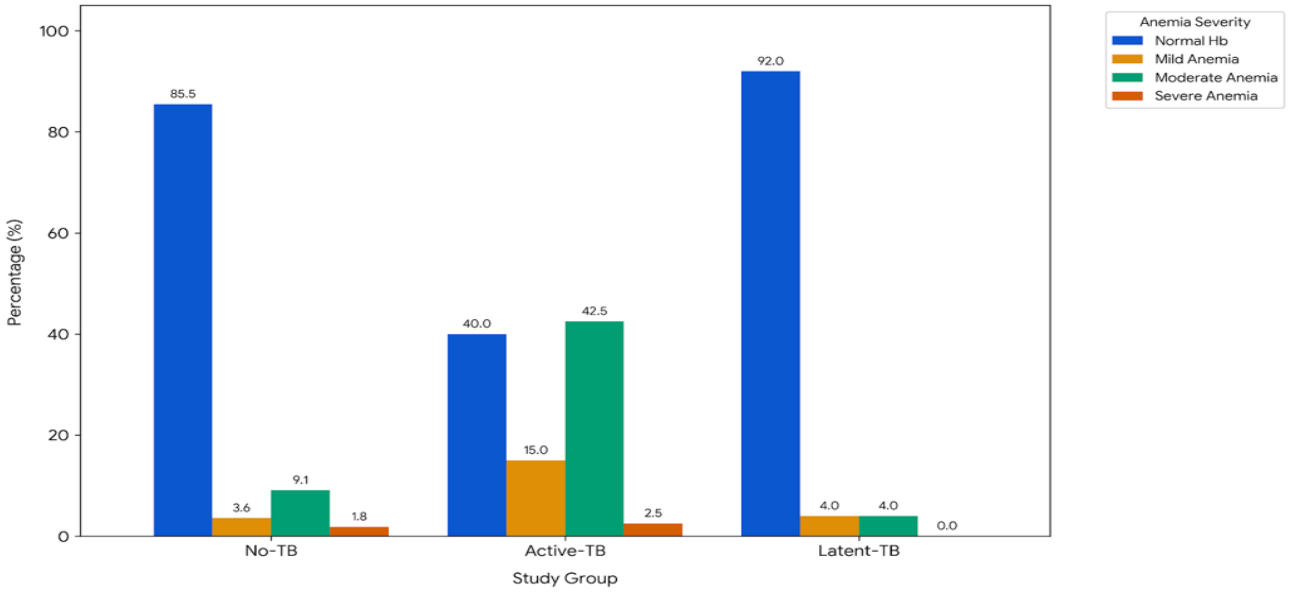

Figure 1: Severity of anemia among study population.

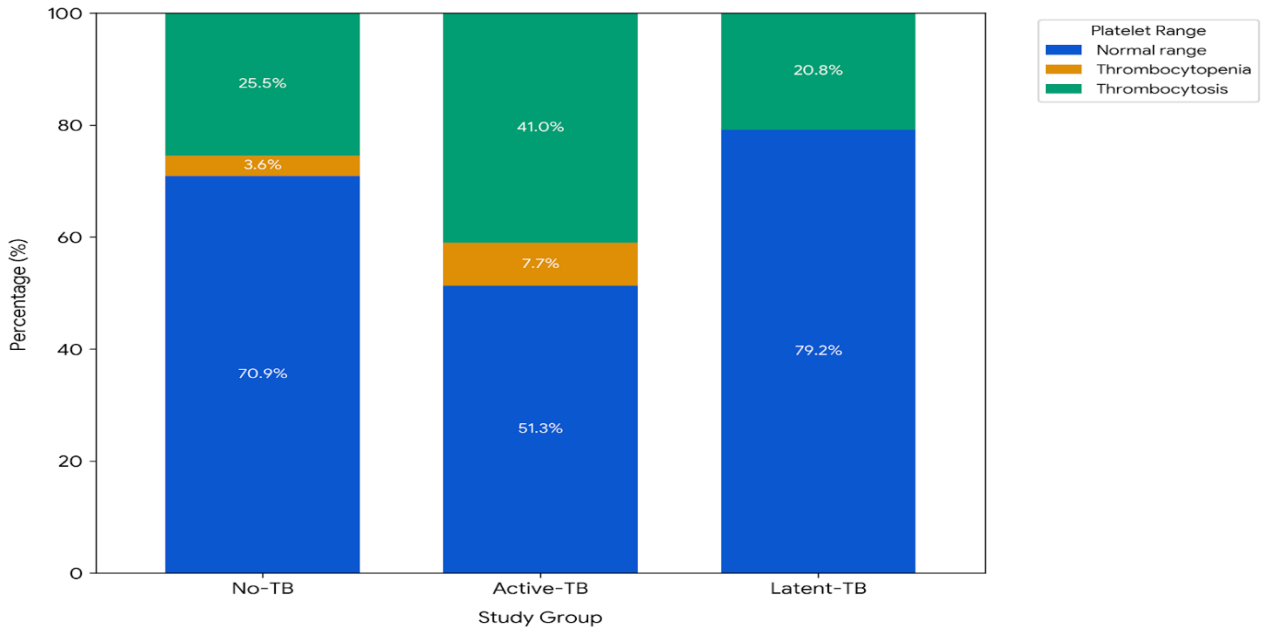

Figure 2: Variation in platelet count among study population.

Hemoglobin and hematocrit

The mean hemoglobin (HB) levels across the study participants were normal at 13.0±2.5 gm/dl (p<0.001), however the active-TB group had lower HB levels (11.3±2.1 gm/dl) compared with the no-TB (13.6±2.3 gm/dl) and latent-TB (14.4±2.0 gm/dl) groups. The hematocrit level of the study participants was generally normal 41.9±7.8% (p<0.001) and comparable across the no-TB (43.7±7.4%) and latent-TB (46.1±5.9%) groups, however was lower in the active-TB (36.7±6.4%) group. The prevalence of anemia across the study participants was 27.5% (mild-27.3%; moderate-66.7% and severe-6.1%). However, among the active-TB group, majority 17 (42.5%) had moderate anemia, 6 (15%) had mild anemia and only 1 (2.5%) had severe anemia (Figure 1).

Platelet count

The mean±SD platelet count for study participants was within normal range at 255.5±101.7x10^9/l (p=0.224) with the active-TB (279.0±131.7x10^9/l) having slightly higher platelet count compared to the latent-TB (244.7±82.8x10^9/l) and no-TB (243.6±79.4x$10^{9/L}$) groups. Among the active-TB group, 14 (41.0%) had thrombocytosis and only 2 (7.7%) had a thrombocytopenia. In the no-TB and latent-TB groups 14 (25.5%) and 5 (20.8%) had thrombocytosis respectively while 2 (3.6%) had thrombocytopenia among the no-TB group and zero in the latent-TB group (Figure 2).

DISCUSSION

Our study aimed to evaluate the hematological parameters among HIV/TB co-infected patients enrolled from both outpatient and inpatient health facility settings in Uganda. The findings revealed significant alterations in several hematological indices among HIV infected patients depending on their TB coinfection status i.e., active-TB, latent-TB and no-TB.

The study participants' hematological profile showed relatively low levels of anemia (27.5%) with the mean hemoglobin levels reported at 13.0±2.5 gm/dl (p<0.001). However, among the active-TB group, anemia was reported among 24 out of 40 (60%) patients with majority having moderate anemia (17/40; 42.5%). This is consistent with findings from other studies that have reported anemia as a common sequalae among TB patients, for example a retrospective cohort study in India reported a 91.6% prevalence of anemia among PLHIV with TB with majority (56.3%) having moderate anemia.[20] Other studies that have reported relatively high rates of anemia among HIV/TB coinfected patients of 80% and 46%.[21,22] The anemia among HIV/TB coinfected patients maybe multipronged, with the infiltration of the bone marrow by both the *Mycobacterium* and HIV pathogens and the resultant suppression of erythropoiesis.[16,23]

The elevated leukocyte and neutrophil counts observed within the active-TB group (5/40; 12.5%; p=0.02) is consistent with findings from other studies that reported leucocytosis and neutrophilia among TB/HIV coinfected patients. For example, a retrospective cohort study in India documented leukocytosis and neutrophilia of 16.3% and 25.2%, p<0.0001 among HIV/TB coinfected patients.[20] These observations are indicative of an active inflammatory response, a known hallmark of tuberculosis infection.[17,24] This is supported by the elevated levels of C-reactive proteins, a marker of inflammation being high in the active-TB group (85%) compared with the latent (12%) and no-TB (23.6%) groups of this study population.

The lymphopenia seen in 37.5% of the HIV/TB coinfected patients of our study participants correlates with findings from other studies that have highlighted reduced lymphocyte count. For example, Kaleem reported up to 90% and Shah reported 16.0% levels of lymphopenia.[19,25] It has been postulated that the observed lymphopenia among TB patients is as a result of MTB induced T-lymphocyte apoptosis, which is indicative of disease severity and progression.[25,26]

Studies have presented conflicting findings on platelet count levels among TB/HIV coinfected patients, with some reporting thrombocytosis as consistent with our study findings.[19,27] The increase in platelet count in TB patients may be attributed to elevated levels of interleukin-6 (IL6), which promotes mega-karyocytopoiesis during the acute phase of infection. However, other studies have documented reduced platelet count among PLHIV coinfected with TB.[20] Moreover, TB infection often leads to malnutrition, and as noted with our study findings, about 40% of the active-TB group patients were underweight compared 10.9% in the no-TB and 12% in the latent-TB groups. This eventually contributes to anemia and other hematological abnormalities.

The strengths of our study lies in a well-defined study population and having comparator groups (latent-TB and No-TB patients) which provides more robust values for the hematological parameters under investigations. The detailed assessment of various hematological parameters provided a comprehensive understanding of the systemic impact of TB, contributing to the growing body of evidence on the utility of hematological markers in TB patients care and monitoring. However, certain limitations must be acknowledged. The cross-sectional nature of the study precludes the establishment of causality between TB and the observed hematological changes. Furthermore, the relatively small sample size, particularly for latent TB group, may limit the generalizability of the findings to broader populations.

We recommend longitudinal cohort studies with larger sample to validate our study findings and to establish any temporal relationship between hematological

abnormalities and TB infection among PLHIV. Integrating routine hematological assessments in high TB burden settings like Uganda, could improve patient monitoring and management, and ultimately reduce TB-related morbidity and mortality.

CONCLUSION

The study demonstrated significant deviations in hematological parameters, particularly hemoglobin, RBC and its related indices (MCV, MCH), WBC, neutrophil and platelet counts, among patients with HIV coinfected with pulmonary tuberculosis. These findings suggest that routine hematological assessments can serve as a simple tool for prognostic monitoring of TB in resource-constrained settings. Integrating these hematological markers into routine clinical evaluations could improve patient management and reduce TB-related complications, thereby enhancing overall healthcare outcomes and contributing to the global TB control efforts.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Infectious Diseases Institute research ethics committee (IDI-REC-2024-84) and also from the Uganda National Council of Science and Technology (HS3933ES)

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