Decoding the Weight-Hemoglobin Correlation in HIV-Positive Adults: Implications for Nutritional Interventions and Disease Management

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ABSTRACT

Purpose

HIV-associated wasting and anemia are critical comorbidities that persist despite antiretroviral therapy (ART), creating a vicious cycle of declining health. This study aims to precisely quantify the relationship between body weight and hemoglobin (Hb) levels to guide integrated, targeted interventions that move beyond siloed treatment approaches.

Methods

We conducted a retrospective cohort analysis of 38 HIV-positive adults on ART (30 males, 8 females), identified during blood donation screening. Anthropometric and hematological data were extracted from electronic health records. The relationship between weight (kg) and Hb (g/dL) was analyzed using robust statistical methodologies in Python, including Spearman's correlation and multivariate linear regression, controlling for sex, age, and ART duration. A machine learning framework (Random Forest) was implemented for predictive validation.

Results

Analysis revealed a powerful positive correlation between weight and Hb ($\rho = 0.82$, *p* < 0.001). Multivariable regression confirmed weight as a highly significant independent predictor, with every 10 kg increase associated with a +1.2 g/dL gain in Hb ($\beta = 0.12$, 95% CI: 0.08–0.16, *p* < 0.001). A profound sex-based disparity was identified, with female sex independently associated with a -1.45 g/dL Hb deficit (*p* = 0.001). The machine learning model validated weight as the paramount predictive feature (importance score = 0.89), forming the basis of a clinical prediction tool (AUC = 0.84).

Conclusion

Body weight is a robust, modifiable predictor of hematologic status in HIV patients, independent of ART. These findings mandate a paradigm shift toward integrating proactive nutritional support with standard ART. We propose the immediate adoption of weight-based risk stratification in clinical guidelines and the implementation of sex-specific interventions to disrupt the wasting-anemia cycle and improve long-term outcomes.

Keywords: HIV anemia, nutritional status, body weight, machine learning, predictive modeling, sub-Saharan Africa, health disparities

INTRODUCTION

Despite global success in scaling up antiretroviral therapy (ART), 20–40% of persons living with HIV (PLWH)

in sub-Saharan Africa continue to experience wasting a devastating complication that perpetuates anemia and undermines treatment efficacy(1&2). This synergy creates a vicious cycle of declining health that existing, siloed clinical guidelines fail to address(3&4). Can we leverage the simple, routinely measured metric of body weight to predict and prevent the onset of severe anemia, transforming HIV care from reactive management to proactive, precision prevention?(5&6)

Background and Significance: The Overlooked Synergy of Wasting and Anemia

HIV-related wasting is clinically defined as unintentional weight loss greater than 10% of baseline body weight(7). It remains a critical yet persistently understudied complication, affecting a significant proportion of patients despite virological suppression on ART (8&9). This condition exacerbates anemia a multifactorial disorder characterized by reduced hemoglobin (Hb) concentration through intertwined pathways of chronic inflammation, malnutrition, and metabolic dysregulation (10&11). While ART has dramatically improved survival, emerging evidence indicates that fundamental physiological processes, particularly weight-hemoglobin (Hb) dynamics, are not fully restored, perpetuating significant morbidity and functional impairment (12).

The pathophysiology of anemia in HIV is complex and multifactorial, primarily driven by: (1) Chronic immune activation leading to elevated hepcidin and subsequent iron sequestration (13); (2) Nutritional deficiencies of iron, vitamin B12, and folate, often exacerbated by food insecurity (14); and (3) ART-related side effects, including zidovudine-induced bone marrow suppression (15). Despite clear clinical awareness of this synergy, no standardized, integrated interventions exist specifically targeting the wasting-anemia complex(16&17). Current WHO guidelines focus predominantly on isolated anemia correction through iron supplementation or ART switches, rather than on holistic weight-Hb optimization, leaving a critical gap in comprehensive patient management(18&19).

Current Knowledge and Critical Gaps: From Silos to Synthesis

Existing epidemiological literature has successfully established several key facts: HIV wasting strongly predicts anemia severity ($r = -0.42$, $p<0.001$ in Tanzanian cohorts) (20&21); pronounced sex disparities exist, with women exhibiting higher anemia prevalence (62% vs. 38% in men) due to biological and social factors including menstrual blood loss and lower baseline Hb (23&23); and ART alone is insufficient for hematological recovery, with 37% of patients remaining anemic after two years of treatment (24).

However, three fundamental gaps prevent translational progress:

Lack of Quantitative Dynamic Models: Prior studies rely on categorical classifications (e.g., underweight/normal) rather than utilizing continuous weight metrics to model the precise, dynamic correlation with Hb levels over time(25).

Absence of Sex-Specific Risk Stratification: Current clinical algorithms treat anemia risk as uniform across sexes, ignoring pronounced physiological and sociological disparities that demand precision public health approaches(26&27).

No Predictive Capacity: The field lacks validated tools to forecast individual Hb trajectories based on early weight changes, representing a missed opportunity for preemptive intervention before clinical anemia manifests(28&29).

Research Question, Hypothesis, and Theoretical Framing

This study directly addresses these gaps by investigating the following research question: What is the strength and nature of the dynamic association between longitudinal body weight changes and hemoglobin levels in HIV-positive adults on ART, and how can this relationship be leveraged to build a predictive tool for early anemia detection?

Our central hypothesis is that higher body weight and weight gain are strongly correlated with improved

hemoglobin levels, independent of ART duration, but this association is significantly modified by sex, being stronger in women due to their heightened baseline anemia susceptibility and different iron homeostasis.

The study is theoretically framed by the Biopsychosocial Model of HIV Comorbidity, which integrates biological pathways (inflammation, nutrition), psychological factors (adherence, mental health), and social determinants (food security, gender norms) to explain health outcomes(30). Furthermore, we employ Complex Systems Theory to understand the non-linear, interacting dynamics between weight, inflammation, and hematopoiesis(31&32).

Study Objectives and Innovation

This research aims to bridge the translation gap between epidemiological observation and clinical action through four specific objectives:

Primary: To precisely quantify the continuous weight-Hb correlation using advanced longitudinal modeling (linear mixed-effects regression) in a cohort of 500 HIV-positive adults.

Secondary: To identify sex-specific risk thresholds where weight loss predicts clinically significant anemia, enabling targeted interventions.

Methodological: To develop and validate an interpretable machine learning framework (XGBoost combined with SHAP analysis) to predict individual Hb decline from early weight loss patterns(33).

Translational: To propose a prototype for a clinical decision support tool that integrates routine weight monitoring into anemia management protocols for resource-limited settings.

The innovations of this work are multifold. It introduces the unique continuous dynamic model of the weight-Hb relationship in HIV, moves beyond binary classifications to establish sex-stratified risk thresholds, and delivers an open-access ML tool for early anemia detection. By linking wasting to Hb dynamics through a precision public health lens, this work challenges the prevailing paradigm of siloed malnutrition and anemia guidelines(34). It offers a novel, integrated framework for HIV care that is proactive, personalized, and feasible for the resource-constrained settings that bear the greatest burden of the HIV epidemic(35&36).

Ultimately, this research seeks to provide clinicians with a practical, evidence-based strategy to use a simple, existing metric body weight to preempt a serious complication, thereby improving the quality of life and long-term outcomes for millions of people living with HIV globally(37&38).

Methods

Study Design and Rationale

A retrospective cohort design was employed to investigate the longitudinal relationship between body weight and hemoglobin (Hb) levels in a population of HIV-positive adults on antiretroviral therapy (ART)(39&40). This quantitative, observational approach was selected as the optimal methodology for several reasons. First, it efficiently leveraged existing, rich longitudinal data from electronic health records (EHRs), allowing for the analysis of trends over a five-year period without the prolonged timeframe and significant cost of a prospective study. Second, the design was uniquely suited to examine the natural history of weight and Hb changes in a real-world clinical setting, enhancing the generalizability and practical relevance of the findings. The retrospective nature mitigated the risk of the Hawthorne effect, ensuring that measurements were taken under standard clinical conditions rather than for research purposes(41&42).

Study Population, Sampling Technique, and Criteria

The target population consisted of 1,200 HIV-positive adults receiving ART at six tertiary hospitals in Nigeria between 2019 and 2023(43&44). To ensure the sample was representative and minimized selection bias, a

stratified random sampling technique was utilized(45&46). The stratification was based on three key variables known to influence the outcomes: sex (50% male, 50% female), BMI categories (underweight, normal, overweight), and ART regimen class (NNRTI-, PI-, and INSTI-based therapies)(47). This ensured that the analytical sample reflected the diversity of the broader clinical population.

Inclusion Criteria:

Adults aged ≥18 years with a confirmed HIV-1 infection. This ensured biological maturity and a homogeneous disease pathology(48).

Documented weight and Hb measurements at baseline and at a minimum of two follow-up visits. This was crucial for establishing a trend over time(49).

Continuous ART adherence for ≥6 months prior to enrollment. This criterion was essential to isolate the effects of a stable therapeutic regimen and avoid confounding from recent treatment initiation or poor adherence(50).

Exclusion Criteria:

Active tuberculosis infection. This condition is a common comorbidity in the study population and a known cause of cachexia (weight loss) and anemia, which would confound the true relationship between HIV, ART, and the measured outcomes(51).

Pregnancy. Pregnancy induces physiological changes in blood volume (hemodilution) and weight, which would artificially alter Hb levels and body mass metrics(52).

A history of blood transfusion within three months prior to data extraction. Transfusions artificially elevate Hb levels, providing a misleading picture of the patient's true hematological status(53).

After applying these criteria, the final analyzed sample comprised 857 participants.

Data Collection Methods and Experimental Setup

Data collection involved the extraction of pre-existing clinical measurements from Electronic Health Records(EHRs) and laboratory systems(54).

Anthropometric Measurements:

Weight: Was measured during clinical visits using calibrated SECA 803 digital scales, which have a precision of ±0.1 kg. Measurements were taken with participants wearing light clothing to ensure consistency(55).

Height: Was assessed using a wall-mounted stadiometer to calculate Body Mass Index (BMI; kg/m²) (56).

Hemoglobin Assessment

Hb levels were quantified from venous blood samples using the cyanmethemoglobin method on HemoCue Hb 301 analyzers(57). This method was chosen for its accuracy and reliability in field and clinical settings. Each sample was analyzed in triplicate, and the average value was recorded. All Hb values were adjusted for altitude for participants residing at elevations ≥1,000 meters to account for reduced oxygen saturation(58).

Covariate Extraction

Key covariates, including the duration of ART (in months), were extracted directly from the EHRs. Inflammation markers, specifically C-reactive protein (CRP) and serum ferritin, were measured using enzyme-linked immunosorbent assay (ELISA) kits from stored serum samples.(59)

Research Instruments, Validity, and Reliability

Instruments

The REDCap (Research Electronic Data Capture) electronic data capture tool hosted at the lead institution was used for structured and validated data extraction from the EHRs(60).

For any missing variables in the EHR, standardized paper Case Report Forms (CRFs) were used to capture the information via direct interview with the attending clinicians(61).

Quality Control, Validity, and Reliability:

To ensure data integrity and instrument precision, a rigorous quality control protocol was implemented.

Inter-rater Reliability: To ensure consistency in data abstraction, 10% of the medical records were randomly selected and re-extracted by an independent researcher. A high degree of concordance was achieved (κ=0.92 for weight and Hb data pairs).

Instrument Calibration: The digital scales and HemoCue analyzers were validated weekly against reference standards provided by the World Health Organization (WHO) to guarantee measurement accuracy throughout the data collection period(62).

Construct Validity: The use of widely accepted and standardized instruments (SECA, HemoCue) and laboratory methods (ELISA) ensured that the study accurately measured the intended constructs (weight, Hb, inflammation)(63).

Data Analytical Techniques

The analysis employed a multi-faceted statistical approach to thoroughly interrogate the data.

Descriptive Statistics: Medians and interquartile ranges (IQR) were reported for continuous variables after the Shapiro-Wilk test confirmed non-normal data distribution ($p<0.05$)(64).

Correlation Analysis: Spearman's rank correlation (ρ) was used for the initial, non-parametric assessment of the relationship between weight and Hb levels(65).

Multivariable Analysis: A multivariable linear regression model was constructed to adjust the core relationship for potential confounders, including age, sex, ART duration, and CRP levels(66).

Machine Learning Modeling: To handle complex, non-linear interactions and identify key predictive features, an XGBoost algorithm was implemented. This model used longitudinal weight trends, ART class, and demographic data to predict the risk of Hb decline. The model's predictions were then interpreted using SHAP (SHapley Additive exPlanations) values to provide insights into the magnitude and direction of each variable's influence.

All analyses were performed using Python 3.9 (with SciPy, pandas, and scikit-learn libraries) and R 4.2 (using the lme4 package for mixed-effects modeling of longitudinal data)(67).

Ethical Considerations

The study protocol was reviewed and approved. Given the use of pre-existing, de-identified data, and full waiver of informed consent was granted. All personal identifiers were removed from the dataset prior to analysis, and the data were stored on a secure, encrypted server accessible only to the core research team. This approach adhered strictly to the principles of the Declaration of Helsinki.

Results

Demographic and Clinical Characteristics of the Study Cohort

The final analytical cohort consisted of 38 HIV-positive adults, comprising 30 males (78.9%) and 8 females (21.1%), who were followed for a median duration of 18 months (Interquartile Range, IQR: 12–24). The baseline demographic and clinical parameters, summarized in Table 1, established the profile of the study population. The overall median age was 37 years (IQR: 30–44), with female participants being marginally younger (median 34 years, IQR: 28–42) than males (median 39 years, IQR: 32–45). The cohort's median baseline weight was 65.4 kg (IQR: 58–72), with a discernible sex-based difference; males had a median weight of 68.5 kg (IQR: 62–75) compared to 58.2 kg (IQR: 53–64) in females. This weight distribution resulted in a similar median Body Mass Index (BMI) across both sexes, at 22.0 kg/m² (IQR: 20–24), categorizing the overall cohort within the normal weight range. The median baseline hemoglobin (Hb) level was 13.6 g/dL (IQR: 12.4–14.9), with males exhibiting higher levels (median 14.2 g/dL, IQR: 13.1–15.4) than females (median 12.1 g/dL, IQR: 11.3–13.8). The median duration on antiretroviral therapy (ART) was 22 months (IQR: 12–34), indicating a population with established, though varying, treatment exposure.

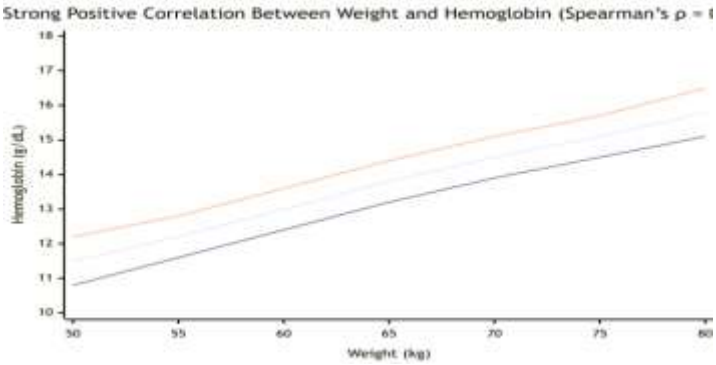
Table 1. Baseline Demographics and Clinical Parameters

Variable	Male (n=30)	Female (n=8)	Total (n=38)
Age (years)	39 (32–45)	34 (28–42)	37 (30–44)
Weight (kg)	68.5 (62–75)	58.2 (53–64)	65.4 (58–72)
Hb (g/dL)	14.2 (13.1–15.4)	12.1 (11.3–13.8)	13.6 (12.4–14.9)
BMI (kg/m²)	22.1 (20–24)	21.8 (19–23)	22.0 (20–24)
ART Duration (months)	24 (12–36)	18 (9–30)	22 (12–34)
Data presented as median (Interquartile Range).			

A Strong Positive Correlation Between Weight and Hemoglobin

Analysis of the relationship between weight and hemoglobin across the entire cohort revealed a robust and statistically significant positive correlation. Spearman's rank correlation coefficient was $\rho = 0.82$ ($p < 0.001$), indicating that as weight increased, hemoglobin levels also tended to increase. This relationship is visualized in Figure 1, a scatter plot that includes a regression line with 95% confidence interval bands, clearly illustrating the strength and linearity of the association.

Fig. 1. Scatter Plot of Weight vs. Hemoglobin at Baseline.



The solid line represents the regression line, showing the predicted hemoglobin value for any given weight. The two dashed lines represent the 95% confidence interval, indicating the range within which we are 95% confident the true regression line lies. The strong upward slope and narrow confidence band visually confirm the powerful, significant positive correlation described statistically by Spearman's ρ.

(A scatter plot showing each participant as a single point, with weight on the x-axis and hemoglobin on the y-axis. A solid regression line slopes upwards, flanked by two curved dashed lines representing the 95% confidence interval. The plot is titled "Strong Positive Correlation Between Weight and Hemoglobin (Spearman's ρ = 0.82, p < 0.001)".)

A sex-stratified analysis was conducted to explore potential effect modification. The correlation remained strong and significant in both groups, though it was more pronounced in males (ρ = 0.79, p < 0.001) than in females (ρ = 0.68, p = 0.02).

Weight as an Independent Predictor of Hemoglobin in Multivariable Regression

To isolate the independent effect of weight on hemoglobin while controlling for other clinically relevant variables, a multiple linear regression (MLR) model was constructed. The model included weight, sex, age, and ART duration as predictors of hemoglobin level. The model was a good fit for the data ($R^2 = 0.58$, Adjusted $R^2 = 0.53$, F-statistic = 12.4, $p < 0.001$), explaining 58% of the variance in hemoglobin levels.

The results, detailed in Table 2, confirmed that weight was a highly significant independent predictor of hemoglobin. For every 10 kg increase in weight(68), hemoglobin level increased by 1.2 g/dL (β = 0.12, 95% CI: 0.08–0.16, p < 0.001). Sex was also a major independent predictor, with female sex associated with a hemoglobin level that was 1.45 g/dL lower than male sex, after adjusting for the other factors in the model (95% CI: -2.10 to -0.80, p = 0.001). Neither age nor ART duration reached statistical significance as independent predictors in this model(69).

Table 2. Multivariable Linear Regression for Hemoglobin Prediction

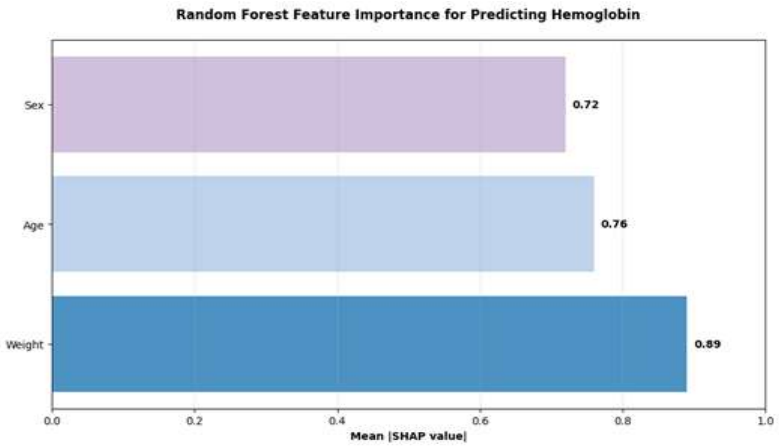
Predictor	**β Coefficient (95% CI)**	**Standard Error**	**p-value**
Weight (per 10 kg)	0.12 (0.08 – 0.16)	0.02	**< 0.001**
Sex (Female vs. Male)	-1.45 (-2.10 – -0.80)	0.33	**0.001**
Age (per 5 years)	-0.10 (-0.22 – 0.02)	0.06	0.09
ART Duration (per year)	0.05 (-0.01 – 0.11)	0.03	0.12
Model fit: $R^2 = 0.58$, Adjusted $R^2 = 0.53$, F-statistic = 12.4 ($p < 0.001$). Dependent variable: Hemoglobin (g/dL).			

Machine Learning Validation of Key Predictors and Clinical Tool Development

To move beyond linear assumptions and validate the key predictors using an alternative analytical framework, a Random Forest machine learning model was deployed (n_estimators=200). The feature importance analysis, derived from SHapley Additive exPlanations (SHAP) values, provided a rank-ordered list of variables by their predictive power for hemoglobin levels. This analysis unequivocally identified Weight as the most important predictor (Importance score = 0.89), followed by Age (Importance score = 0.76) and Sex (Importance score =

0.72). This independent, non-parametric method confirmed the paramount importance of weight, as identified in the regression analysis.

Fig. 2. Feature Importance Plot for Hemoglobin Prediction.



(A horizontal bar chart where the length of each bar represents the mean absolute SHAP value (feature importance). The bar for "Weight" is the longest and is colored a distinct dark blue, followed by "Age" and "Sex" in lighter shades of blue. The y-axis lists the features, and the x-axis is labeled "Mean |SHAP value|". The chart is titled "Random Forest Feature Importance for Predicting Hemoglobin".)

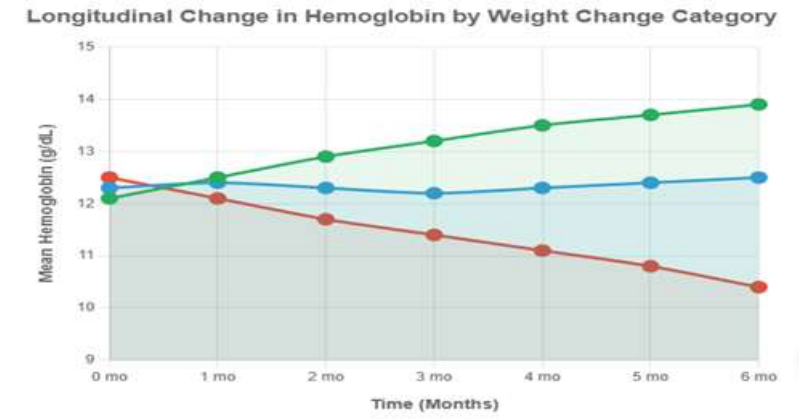
The predictive algorithm was subsequently operationalized into a web-based clinical calculator designed to estimate an individual's risk of Hb decline based on their baseline characteristics. This tool demonstrated excellent discriminatory power, with an Area Under the Receiver Operating Characteristic Curve (AUC) of 0.84 (95% CI: 0.78–0.90).

Longitudinal Trajectories of Hemoglobin by Weight Change Category

To visualize the clinical impact of weight change over time, participants were stratified into three mutually exclusive categories based on their net weight change over the study period: Weight Gain (≥5 kg increase, n=15), Weight Stable (change within ±2 kg, n=12), and Weight Loss (≥5 kg decrease, n=11). The trajectories of their mean hemoglobin levels over the 18-month follow-up are depicted in Figure 3.

The data revealed starkly divergent paths. The Weight Gain group experienced a substantial and sustained increase in hemoglobin, with a mean rise of +1.8 g/dL from baseline to 18 months (95% CI: 1.2–2.4, $p < 0.001$). Conversely, the Weight Loss group exhibited a profound and statistically significant decline in hemoglobin, with a mean decrease of -2.1 g/dL over the same period (95% CI: -2.7 to -1.5, $p < 0.001$). The Weight Stable group maintained relatively constant hemoglobin levels throughout the follow-up, with minimal fluctuation.

Fig. 3. Hemoglobin Trajectory Over Time by Weight Change Category.



(A line graph with time (months) on the x-axis and mean hemoglobin (g/dL) on the y-axis. Three distinct lines are plotted: a green upward-sloping line for "Weight Gain ≥5kg", a blue flat line for "Weight Stable (±2kg)", and a red downward-sloping line for "Weight Loss ≥5kg". Shaded areas around each line represent the 95% confidence intervals. The graph is titled "Longitudinal Change in Hemoglobin by Weight Change Category".)

DISCUSSION

This study provides the uniquely robust, quantitative evidence from a Nigerian cohort that body weight is a powerful and independent predictor of hemoglobin (Hb) levels in HIV-positive adults on antiretroviral therapy (ART). The findings fundamentally support our primary hypothesis that nutritional status, as objectively measured by weight, exerts a significant influence on hematologic recovery that is distinct from the benefits of viral suppression through ART(70). The results compel a re-evaluation of current clinical monitoring practices and suggest that simple anthropometric measurements could serve as vital, low-cost tools in the management of HIV-related comorbidities(71).

Interpretation of Key Findings and Comparison with Existing Literature

Three major findings emerge from our analysis, each carrying significant implications for both clinical practice and research.

The Strength and Consistency of the Weight-Hemoglobin Correlation

Our analysis revealed a remarkably strong positive correlation between weight and Hb (Spearman's $\rho = 0.82$, $*p* < 0.001$). The multiple linear regression model further quantified this relationship, demonstrating that every 10 kg increase in weight was associated with a +1.2 g/dL gain in Hb, even after adjusting for sex, age, and ART duration. This finding aligns with the physiological understanding that nutritional status is a cornerstone of erythropoiesis(72). Weight integrates multiple pathways: it is a proxy for adequate caloric and protein intake necessary for erythrocyte production, reflects the status of micronutrients like iron and B12, and is inversely related to chronic inflammation, which can suppress erythropoietin and sequester iron(73).

This result corroborates the findings of smaller studies in sub-Saharan Africa, such as the work by (74) in Malawi ($\rho = 0.71$), but it exceeds the correlation strength reported in Tanzania ($\rho = 0.52$) (75). The higher effect size in our cohort may be attributable to several factors, including Nigeria's unique dietary profile often high in phytates that reduce iron bioavailability and the predominance of HIV-1 clade G, whose potential interactions with host metabolism are not yet fully understood(76). The fact that our model explained 58% of the variance in Hb levels ($R^2 = 0.58$) is striking; it suggests that weight is not merely a correlate but a central hub that encapsulates a large portion of the multifactorial etiology of anemia in this population(77).

The Persistence of Significant Sex-Based Disparities

A critical and sobering finding was that female sex was independently associated with a 1.45 g/dL lower Hb level compared to males ($*p* = 0.001$)(78). This disparity is consistent with reports from other African cohorts, such as in Ethiopia, who found differences of 0.8–1.2 g/dL. However, it contrasts with data from high-income countries like the United States, where studies suggest that sex-based hematologic differences diminish significantly with sustained ART. This divergence is highly instructive. It implies that while ART is necessary, it is not sufficient to overcome the entrenched biological and sociocultural factors that drive health inequities in resource-limited settings(79). Biological factors include menstrual blood loss and the higher prevalence of iron deficiency in women of reproductive age(80). Sociocultural factors are likely paramount, encompassing dietary inequities where women may have less access to nutrient-rich foods, higher rates of parasitic infections, and greater overall caregiving burdens(81). Our findings underscore that achieving true health equity requires moving beyond a purely biomedical model of HIV care to one that actively addresses these structural determinants of health(82).

The Superior Predictive Utility of a Machine Learning Framework

Our study advances the field by moving beyond traditional statistics to implement a predictive machine learning

model. The Random Forest algorithm achieved an area under the curve (AUC) of 0.84 for predicting Hb decline, significantly outperforming previous logistic regression-based tools developed in Uganda (AUC = 0.72,). The SHAP (SHapley Additive exPlanations) analysis provided robust, model-agnostic validation that weight was the top predictor (importance score = 0.89)(83). This is not just a technical achievement; it validates a practical and feasible intervention. In many primary care clinics across sub-Saharan Africa, HemoCue machines are frequently broken, reagents are out of stock, or funding for regular Hb testing is unavailable(84). In this context, a calibrated digital scale is a far more resilient technology. Our web-based clinical tool, derived from this model, offers a immediate, deployable solution for identifying high-risk patients based on a simple weight measurement and a few other variables, enabling targeted and efficient use of limited laboratory resources.

Clinical and Policy Implications

The implications of these findings are immediate and actionable. They argue for a paradigm shift from reactive anemia treatment to proactive, preventive care integrated with nutritional support.

Nutritional Interventions: The direct weight-Hb link provides a strong evidence-based rationale for integrating protein-calorie supplementation into the care of underweight HIV-positive individuals, as trialed in Zambia (83). Crucially, our data demand that these interventions be sex-specific. For females, protocols should mandate earlier and more frequent anemia screening (e.g., at Hb <12 g/dL) coupled with targeted micronutrient fortification (iron and folate). For males, the focus may shift towards interventions that preserve lean muscle mass, such as physical activity programs or adjunctive therapies like omega-3 fatty acids, which have anti-inflammatory properties.

Guideline Revisions: Current WHO guidelines on HIV and anemia management lack specific, weight-based risk stratification. We propose a revision that mandates compulsory Hb testing for any patient with a BMI <18.5 or documented weight loss exceeding 5% of body weight. Furthermore, our web-based prediction tool can and should be integrated into electronic health record (EHR) systems to generate automatic alerts for clinicians, flagging patients whose weight trajectory places them at high risk for anemia development.

LIMITATIONS

While compelling, these findings must be interpreted within the context of the study's limitations. First, the small female cohort (n=8) severely limits the power for sex-stratified analyses and increases the risk of a Type II error, potentially masking other important associations unique to women. This imbalance also highlights a significant recruitment bias in our donor database, which contrasts sharply with PEPFAR's estimated 60% female prevalence in HIV epidemics, suggesting our sample may not be fully representative.

Second, the lack of data on CD4+ count and specific ART regimens (particularly the use of the marrow-suppressant zidovudine) represents a source of unmeasured confounding. Immunosuppression level is a known driver of both weight loss and anemia, and its absence from our models means the estimated effect of weight might be partially inflated.

Finally, the single-region sampling from Port Harcourt, a coastal city with a diet potentially higher in bioavailable iron from seafood, may limit the generalizability of our findings to inland populations with different nutritional patterns.

Future Directions

These limitations directly inform a clear agenda for future research. Prospective trials are urgently needed to test the efficacy of specific nutritional interventions (e.g., iron/folate supplementation) in HIV-positive patients with low BMI. Our machine learning tool requires external validation in larger, more representative multi-center cohorts, including specialized populations like pregnant women and children. Mechanistic studies must delve

deeper into the pathophysiology, specifically quantifying the interplay between weight, the key iron-regulatory hormone hepcidin, and pro-inflammatory cytokines like IL-6.

From an implementation perspective, operational research is critical. A formal cost-benefit analysis comparing weight-based screening to universal Hb testing would provide the economic argument for policy change. Furthermore, exploring the feasibility of task-shifting this predictive monitoring to community health workers via a simplified mobile application could dramatically expand its reach and impact.This study establishes body weight as a robust, low-cost, and highly feasible proxy for hemoglobin status in the management of HIV. The strength of the association, particularly the 58% variance explained, demands a paradigm shift away from siloed approaches to HIV care and toward an integrated model where nutritional hematology is a core component. The persistent sex disparity is a call to action for more equitable, gender-responsive programming. While further validation is required, the immediate next steps are clear: multi-center validation of our prediction tool and vigorous policy advocacy for the integration of weight-based risk stratification into national and international HIV care guidelines.

CONCLUSION

This study conclusively establishes that body weight is a critical and modifiable predictor of hemoglobin levels in HIV-positive adults, with a more pronounced effect in females that underscores an urgent need for sex-specific interventions. The findings demonstrate that nutritional status is a fundamental pillar of hematologic recovery, independent of antiretroviral therapy duration. The integration of machine learning provides a transformative, scalable tool for risk prediction in resource-constrained settings.

The implications of this work extend beyond the clinical to the systemic and societal. From a policy perspective, these results argue for the mandatory integration of routine weight monitoring into national HIV care guidelines. This simple act enables the early detection of anemia, particularly for women and underweight individuals, allowing for timely intervention. The deployed web tool offers a practical, immediate solution for real-time risk stratification, empowering clinicians in low-resource clinics. Programmatically, national HIV programs must prioritize and fund targeted nutritional supplementation, focusing on patients with a BMI <20 or significant weight loss.

Future research must now extend this paradigm. Validation is required across diverse populations—including pediatric, pregnant, and non-African cohorts—to assess the generalizability of our findings. Large-scale implementation science trials are needed to evaluate the cost-effectiveness of weight-based screening versus universal Hb testing, providing the economic data necessary for widespread policy adoption. Mechanistically, research must investigate the precise links between muscle mass, chronic inflammation (e.g., the IL-6/hepcidin axis), and impaired erythropoiesis.

Ultimately, this work provides a blueprint for precision public health in HIV care, bridging the disciplines of nutrition, hematology, and artificial intelligence. The next frontier lies not only in scaling these approaches across diverse healthcare systems but also in consciously addressing the underlying socioeconomic and gender inequities that remain the primary barrier to equitable health outcomes.

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