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Under-nutrition and its associated factors among adult second-line antiretroviral treatment users in Northern Ethiopia

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Abstract

Background Despite advancements in Human Immunodeficiency Virus (HIV) treatment and care, undernutrition remains a significant concern, accelerating disease progression and risk of Acquired Immune Deficiency Syndrome (AIDS)-related deaths. The nutritional status of second-line antiretroviral treatment (SLART) users in Ethiopia has not been thoroughly investigated. So, this study aimed to assess the nutritional status of HIV/AIDS patients who were on SLART and its associated factors in Northern Ethiopia.

Methods A retrospective cross-sectional study was conducted on 366 HIV-infected adults who had been on SLART for at least six months in northern Ethiopia. Clients who had documented Weight and height at six months of therapy were included. Data was entered and cleaned by using EpiDATA version 4.6.0.2 and statistical analysis was done by STATA version 17. Multiple imputation method was applied to manage variables having up to 25% missing values by using R-Version 3.6.2 software. Binary logistic regression was used with $P < 0.05$ as a significant predictor in the final analysis. Data was collected from February 01 to April 30, 2021.

Results The magnitude of undernutrition among adults who were on SLART in the study area was 38.52% (95%CI: 33.65–43.64). Those populations also had a baseline undernutrition status of 39.1% (95%CI: 34.11–44.15) during their transition to SLART. The risk of being malnourished at six months of SLART initiation was fifteen times higher among those who were undernourished at SLART start (AOR:15.099, 95%CI: 8.532, 26.720) reflecting the high burden of the problem in the advanced courses of HIV/AIDS treatment and care.

Conclusions The proportion of undernutrition among SLART users in Northern Ethiopia is high. During HIV therapy, a client's overall nutritional health is predicted by their prior undernutrition condition. This highlights the need for comprehensive nutritional assessment, counseling, and monitoring of the nutritional status of SLART users in the area with emphasis on an early identification of possible barriers to the improvement of such conditions. Promoting the consumption of nutrient-dense local foods and appropriate food preparation methods in addition to nutritional support are vital in this setting.

Keywords Adult, Antiretroviral, Ethiopia, Secondline, Treatment, Undernutrition

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Background

Despite the advancements in treatment, diagnosis, and supportive care in Human Immunodeficiency Virus (HIV) infections, many Acquired Immune Deficiency Syndrome (AIDS) deaths are associated with malnutrition and its management [1]. Human Immunodeficiency Virus plays a significant role in the development of malnutrition through multifaceted ways. Firstly, low dietary intake, loss of appetite, mouth ulcers, and food insecurity, cause weight loss which leads to severe and moderate malnutrition. Secondly, because of the malabsorption of macronutrients and altered metabolism infected individuals could be malnourished [2].

Undernutrition is common among HIV patients in the poorest regions, including Ethiopia [3]. Its prevalence among adult HIV-positive individuals in Sub-Saharan Africa (SSA) reaches 23.72% [4]. There is a shred of evidence in Ethiopia regarding the burden of undernutrition in HIV/AIDS care among adult populations. It ranges from 16 to 29% in Southern and Central Ethiopia ([5–9], 22.2% in Chiro [10], 23.6% in West Shewa Zone [11], 42.9% in Tigray [3], and 23.2% in Dembia district [12]. A systematic review and meta-analysis of evidence also showed that more than one-fourth (26-27.4%) of HIV-infected adults receiving ART are undernourished [13, 14] with higher prevalence in the Northern and Central parts of the country [13].

Different causes and risk factors are contributing to the development of adult undernutrition in HIV/AIDS care. One of the main nutritional issues with HIV-positive patients is their low dietary diversity [15, 16] as the majority of those afflicted did not maintain a healthy diet, which could have an impact on their immune system, which HIV is already attacking [17]. Lack of ready-to-use therapeutic feeding (RUTF), advanced clinical stage, development of gastrointestinal symptoms like diarrhea, not taking cotrimoxazole preventive therapy (CPT), tuberculosis (TB) infection, food insecurity, poor ART adherence, low CD4 count, substance use, longer ART duration and low monthly income [3, 6, 7, 11, 13, 18, 19]. Undernutrition is twice as likely to occur when OIs and other comorbidities including anemia and eating disorders present. Furthermore, social support lowers the risk by 36% [20]. Among HIV-infected populations, the prevalence of food insecurity may also exceed 80% which affects their nutritional status, medication adherence, and missing appointments which all affect treatment outcomes [21–23]. The impact of depression [24], high family size [19, 25], and low economic status also play a significant role in the development of undernutrition in HIV/AIDS care and treatment [8].

The Ethiopian government recognized the impact of malnutrition on the outcome of HIV/AIDS treatment and developed guidelines stating that individuals with HIV should consume up to 20% more energy (420 kcal) per day in addition to the National Guidelines for Comprehensive HIV Treatment and Care. This was an attempt to address the nutritional issues faced by HIV-positive individuals [26]. Undernutrition accelerates the progression of disease and the risk of AIDS-associated mortality [27]. A piece of evidence showed that a unit increment in weight reduces the rate of second-line ART (SLART) failure by 8% [18] and low BMI is also associated with virological failure [28]. Undernutrition also increases the probability of lost to follow-up (LTFU) [29] which might affect the level of adherence and be associated with 60% of HIV/AIDS-related mortality in Ethiopia [30]. Improved nutritional problems and better quality of life are the results of nutritional interventions in HIV care [31]. Knowledge of essential components of nutrition and incorporating them in the management goes a long way in improving quality of life and better survival in HIV-infected patients [1]. For food-insecure people with chronic illnesses, comprehensive, medically appropriate food support may enhance several health outcomes [32].

Despite undernutrition being among the over-researched areas in HIV care in Ethiopia, the focus of previous research was on first-line regimens and children [4, 13, 14] highlighting the need for further research in advanced HIV care. Long-term sustainability in assessing the nutritional well-being of HIV-positive patients is a key component of HIV care nutrition programs [31]. Therefore, this study aimed to assess the nutritional status of HIV/AIDS patients who are on SLART and its associated factors in Northern Ethiopia.

Methods

Study area and period

The study was conducted in health facilities found in North Wollo and Wag Hemra Zone, Amhara region, Ethiopia. North Wollo Zone is boarded by Wag Hemra to the north, South Wollo to the south, South Gondar to the west, Tigray Region to the northeast, and Afar Region to the east with nearly two million populations [33]. Woldia is the town for the North Wollo Zone, found 521 km northeast of Addis Ababa on the highway to Mekelle. Wag Hemra Zone's zonal center is Sekota. Wag Hemra borders the Tigray Region to the north and east, South Gondar to the southwest, North Gondar to the west, and North Wollo to the south with an estimated population of over half a million (https://en.wikipedia.org/wiki/Wag_Hemra_Zone). Three Hospitals namely Woldia Comprehensive Specialized Hospital, St. Lalibella General Hospital, and Tefera Hailu Memorial Hospitals were providing SLART before April 2020 in North East Amhara for a population of 493 HIV-infected individuals of which 366 were adults (Hospitals HMIS data, Sep 2020). The study was conducted from February 1, 2021, to April 30, 2021.

Study design
Institution-based retrospective type of cross-sectional study was conducted.

Study population
All HIV-infected clients who were on SLART in health facilities found in North Wollo and Wag Hemra Zones.

Inclusion criteria
Adult clients who were on SLART and have documented Weight and height at six months of treatment initiation. Six months is the usual duration, as this cutoff was established by clinical expert consensus to accommodate patients who are stable and under good clinical management with their present treatment plan [34]. Furthermore, in HIV care, treatment failure (clinical, immunological, or virological) is diagnosed six months after the start of treatment [35].

Exclusion criteria
Clients who had no documented SLART initiation date.

Sample size determination and sampling technique
The sample size was calculated by using a single proportion formula by taking the magnitude of undernutrition among SLART users as 50%, 95% confidence level, and 5% marginal error. The final sample size reached 384 HIV-infected adults on SLART. However, the total adult population meeting the eligibility criteria was 366 as a result universal sampling technique was applied.

Data collection methods
Data were retrieved from the participants' charts and medical records by using a structured data extraction checklist. Socio-demographic and clinical information of clients were extracted.

Outcome variable Under-nutrition among SLART users (Yes/No).

Independent variables Socio-demographic characteristics (age, sex, educational status, marital status, residence, Occupation), duration on ART, WHO clinical staging, functional status, presence of opportunistic infections (OIs) including TB, drug adherence, TB prophylaxis, CPT use, baseline BMI and disclosure status.

Operational/ definition of terms
Undernutrition defined as a BMI of below 18.5 kg/m^2. The patient's BMI was calculated by using the weight of the study subjects measured in kilograms divided by the height in meters square [36].

Adult individuals whose age is 18 and above [36].

Second-line antiretroviral treatment The use of a boosted protease inhibitor (bPI) plus two nucleoside analogs (NRTIs) for treatment in HIV care [37].

Adherence The level of ART drug adherence was classified as **Good** if ≥95% adherence by pill count, **Fair** if 85–94% adherence by pill count, or **Poor** if <85% adherence by pill count.

WHO clinical staging
Stage-I: When an HIV-infected individual is asymptomatic/having Persistent generalized lymphadenopathy. **Stage II**: presence of moderate and unexplained weight loss/ recurrent respiratory tract infections. **Stage III**: detection of opportunistic infections like TB. **Stage IV**: the presence of AIDS-defining illness/HIV wasting syndrome [38].

Functional status
Working: Able to perform usual work inside or outside the home. **Ambulatory**: Able to perform Activities of Daily Living (ADL), Not able to work. **Bedridden**: Not able to perform ADL [39].

Data quality control
Data were collected after having a 5% preliminary review of the sample and one-day training of data collectors and supervisors.

Data processing and analysis
Data was entered and cleaned by using EpiDATA version 4.6.0.2 and statistical analysis was done by STATA version 17. Multiple imputation method was applied to manage variables having up to 25% missing values by using R-Version 3.6.2 software. Binary logistic regression was used for the analysis with a p-value of ≤0.25 in the bivariable analysis and a p-value<0.05 with a 95% confidence level was considered significant in the final regression model.

Results
Data from 366 eligible study subjects' were analyzed. The average age of study participants was 41.24(SD±10.12) years. The majority of the study subjects were below the age of 42 (50.8%) and were urban residents (61.2%). More than three-fourths of the participants were ever married (77.3%) and disclosed their HIV status (93.2%) (Table 1).

Nutritional and clinical characteristics of participants
About 39.1% (95%CI: 34.11–44.15) of the participants were undernourished during second-line treatment initiation. The mean BMI level at SLART initiation was 19.914 kg/m^2 (±0.167SD). Around 82% and 89% of participants had good SLART adherence and working status

Table 1 Socio-demographic characteristics of study participants on undernutrition and its associated factors among HIV-infected individuals who are on SLART in Northern Ethiopia

Variables	Variable category	Frequency	Percentage
Age in years	< 42	186	50.8
	41 and above	180	49.2
Sex	Male	200	54.6
	Female	166	45.4
Educational Status	No education	180	49.1
	Primary	121	33.1
	Secondary and above	65	17.8
Residence	Urban	224	61.2
	Rural	142	38.8
Marital Status	Single	83	22.7
	Ever Married	283	77.3
Religion	Orthodox	308	84.2
	Other	58	15.8
Occupational Status	House Wife	78	21.3
	Farmer	99	27.0
	Merchant	83	22.7
	Government employee	64	17.5
	Other	42	11.5
HIV Disclosure status	Disclosed	341	93.2
	Not disclosed	25	6.8

at second-line ART initiation respectively. Around 18% of participants developed opportunistic infections (OIs), of which 10% were respiratory. More than half (52%) of the subjects were on ART for six years or less. (Table 2).

Undernutrition and its associated factors among SLART users in Northern Ethiopia

According to the result of this study, the magnitude of adult undernutrition among SLART clients is 38.52% (95%CI: 33.65–43.64). Accordingly, the patient's previous malnutrition status increases the risk of second-line undernutrition by more than 15-fold (Table 3).

Discussion

A low BMI is linked with undernutrition-related immune system dysfunction, higher vulnerability to opportunistic infections, and metabolic and cardiovascular dysregulation which are all related to poor immunological recovery and increased mortality in HIV care [40].

The magnitude of undernutrition among SLART patients in northern Ethiopia was 38.52% (95%CI: 33.65–43.64) which is consistent with the previous study in Tigray (42.9%) [36] and Jimma (34%) [41]. However, the finding is higher than a study conducted in Nepal (18.3%) [42], South Africa (13%) [43], the systematic review and meta-analysis result of adult undernutrition in SSA countries (23.72%) [4], in Chiro Hospital (22.20%) [44] and a study in Southern Ethiopia (24.1%) [45]. This might be due to the differences in the study population whereby only recently diagnosed patients were included in the South African study and also this study included only patients who have follow-up in second-line HIV care with protease inhibitor (PI) based regimens. A study in adolescents and children revealed that PI-based regimens increase the occurrence of being underweight [46]. In PI-based regimens, drug-induced gastrointestinal side effects, such as diarrhea, are often encountered issues [47, 48] which could increase the risk of undernutrition. The majority of HIV-positive individuals did not eat a healthy diet, which could have an impact on their immune system which is already being attacked by HIV and possibly lead to new infections [17]. In addition, the high prevalence of low dietary diversity and household food insecurity may contribute to the higher magnitude [11, 15]. A study conducted in Ethiopia showed that the magnitude of food insecurity among HIV clients is 62.4% [49]. In addition, the prevalence of undernutrition among the general adult populations in Ethiopia is more than 20% [50, 51] reflecting the high undernutrition burden over HIV-infected individuals in advanced care and treatment.

The effect of undernutrition in HIV care is significant. The immune system is compromised in all aspects by malnutrition. Its performance is also negatively impacted by deficiencies in important micronutrients such as iron, folic acid, zinc, selenium, and vitamins A, C, and D [52]. Undernutrition doubles the risk of HIV-related death [53]. Undernutrition dramatically reduces the time it takes for OIs to develop suggesting that several low-cost nutritional interventions, such as regular nutritional interventions and education, can reduce the incidence of OIs in this susceptible group [54, 55]. These OIs could

Table 2 Clinical characteristics of participants on undernutrition and its associated factors among HIV-infected individuals who are on SLART in Northern Ethiopia

Variables	Variable category	Frequency	Percentage
SLART regimen drug adherence	Good	301	82.2
	Moderate	24	6.6
	Poor	41	11.2
WHO clinical T-stage at SLART initiation	T1	272	74.3
	T2	57	15.6
	T3 and above	37	10.1
History of comorbidities	Yes	31	8.5
	No	335	91.5
Functional status at SLART initiation	Ambulatory/bedridden	42	11.5
	Working	324	88.5
History of OIs during SLART regimen	Yes	67	18.3
	No	299	81.7
Respiratory OIs	Yes	37	10.1
	No	329	89.9
History of taking INH prophylaxis	Yes	197	53.8
	No	169	46.2
History of taking CPT	Yes	319	87.2
	No	47	12.8
Baseline BMI at second-line ART ($N=364$)	< 18.5	142	38.8
	18.5-24.99	201	54.9
	25.0 and above	21	5.7
Duration on ART	≤ 6 years	190	51.9
	> 6 Years	176	48.1
Baseline BMI at SLART initiation ($N=364$)	< 18.5	142	39.01
	18.5-24.99	201	55.22
	≥ 25	21	5.77

Table 3 Determinants of undernutrition among SLART users in Northern Ethiopia

Variables	Variable category	COR(95%CI)	AOR(95%CI)
Age in years		0.985(0.955, 0.992)	0.987 (0.958, 1.017)
Marital Status	Single	1	
	Ever Married	0.636(0.388, 1.043)	0.998(0.495, 2.011)
HIV status disclosure	Yes	0.068(0.205, 1.058)	0.682(0.239, 1.951)
	No	1	1
Second-line regimen adherence	Good	1	1
	Moderate	1.042(0.441, 2.460)	1.189(0.391, 3.618)
	Poor	2.011(0.455, 0.728)	1.277(0.538, 3.031)
WHO T stage at SLART initiation	T1	1	1
	T2	1.799(1.011, 3.200)	1.236(0.593, 2.577)
	T3 & T4	1.765(0.884, 3.523)	1.107(0.438, 2.795)
INH prophylaxis	Yes	1	1
	No	1.443(0.945, 2.202)	1.235(0.712, 2.143)
Baseline BMI	< 18.5	16.762(9.646, 29.128)	**15.099(8.532, 26.720)***
	18.5-24.99	1	1
	≥ 25	22.528(7.589, 66.874)	**22.092(7.308, 66.782)***
ART duration in years		1.060(0.997, 1.127)	1.032(0.952, 1.118)

COR-Crude odds ratio, AOR-Adjusted odds ratio, *-$p<0.0001$

increase hospitalization and inpatient mortality rates to 11.2% [56] and SLART failure [57]. The OIs are one way that HIV/AIDS can directly or indirectly contribute to malnutrition [52]. Poor nutrition also increases the risk of poor ART drug adherence [58] which lowers viral suppression and escalates drug-resistant genetic variants of HIV [59] and poor immune reconstitution secondary to deficient nutritional status [60] and affects immune

function that can reverse the progression of disease [52] which all contributes to the high SLART failure [61] and mortality rate from the disease [62]. Low BMI, poor adherence, and OIs raise the risk of SLART failure by seven, six, and four times respectively [63].

Based on the result of this study, the status of undernutrition among SLART patients is persistently evidenced by its magnitude which was 39.01 at SLART initiation and 38.52% after six months of follow-up reflecting the high burdens of the problem in HIV care and its significant association in second-line regimens [64]. This result was supported by a study conducted in North West Ethiopia that showed a recovery time from undernutrition to over six months in HIV care [65]. This might be due to the low dietary diversity among HIV patients [66] as a result of household food insecurity [67], poor drug adherence, and advanced disease stage at treatment initiation [65]. Nutritional problems in HIV care may be the direct and indirect effects of treatment [7] as ART medications are increasingly known to cause malnutrition in a variety of ways [52]. Moreover, the high prevalence of non-response (67.4%) and defaulting to nutritional programs (70%) could contribute to the high burden of SLART undernutrition [68].

The high prevalence of undernutrition among SLART users could lead to second-line treatment failure [18] and therefore deliberate efforts are urgently needed in HIV care through improving their nutritional status by enhancing nutritional education and support, and by strengthening enhanced adherence counseling [69, 70]. The provision of appetite stimulants (hormones and anabolic agents), recombinant adipokines, and micro/macronutrient supplemental feeding have demonstrated benefits for weight gain and metabolic health in HIV/AIDS treatment and care [40].

Limitations of the study

Though this study tried to assess the magnitude of undernutrition among HIV-infected individuals who were on SLART, due to its retrospective nature important nutritional parameters like individual dietary diversity score, food insecurity, knowledge of good quality food, barriers to the use of prescribed nutritional recommendations or supplements were not addressed. Furthermore, which PI medications contribute to the high magnitude of undernutrition was not assessed. A prospective study should also be conducted to address the effectiveness of enhanced adherence counseling and nutritional interventions on the improvement of patient's nutritional status in advanced care.

Conclusions

The magnitude of undernutrition among SLART users in Northern Ethiopia is high. The problem is also persistent. Accordingly, priorities should be given to nutritional counseling, support, and monitoring of the nutritional status of SLART users in the area with emphasis on optimum local food choices and preparation methods. Identifications of the reason why the problem is persistent should be explored. Based on the availability of nutritional supports, ready-to-use therapeutic feeding and lipid-based nutritional supplements should be provided with close monitoring. Taking individual and contextual factors into consideration in program design, planning, and implementation is essential if the nutritional program in HIV care services is to achieve its goal of addressing malnutrition among people living with HIV.

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Author contributions
SAM, AAK, GFM, and FWF: Conceptualization, Methodology, Software, Data curation, Writing Original Manuscript Draft. MWK, TMD, and AKG.: Software, Validation, Visualization, Investigation. FKB: Supervision, Writing, Reviewing, and Editing. All authors read and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
To conduct the study, permission and an ethical approval letter was obtained from Woldia University's institutional research ethical review (IRB) board. The board approves all the study protocols. A waiver for informed consent was received from the University IRB as the study nature was retrospective type.

Consent for publication
This manuscript doesn't contain any individual/personal data in any form; so it doesn't need consent for publication.

Competing interests
The authors declare no competing interests.

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