Patient Preference and Adherence

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Health-Related Quality of Life and Associated Factors Among Adult HIV Mono-Infected and TB/HIV Co-Infected Patients in Public Health Facilities in Northeast Ethiopia: A Comparative Cross-Sectional Study

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Tilahun Hailu[1]
Mezgebu Yitayal[2]
Lake Yazachew[2]

[1]Department of Health System, School of Public Health, College of Health Sciences, Mekelle University, Mekelle, Ethiopia; [2]Department of Health Systems and Policy, Institute of Public Health, College of Medicine and Health Sciences, University of Gondar, Gondar, Ethiopia

Purpose: This study was conducted to assess the health-related quality of life and associated factors among adult human immunodeficiency virus (HIV) mono-infected and tuberculosis (TB) and HIV co-infected patients in the public health facilities of northeast Ethiopia.

Methods: A comparative facility-based cross-sectional study was conducted from February 01 to May 30, 2019. A total of 434 HIV mono-infected and 143 TB/ HIV co-infected patients were randomly selected for the study. The data were collected using an interviewer-administered structured questionnaire. The health-related quality of life of patients was measured using the World Health Organization quality of life HIV instrument which contains physical, psychological, social relationships, environmental, level of independence, and spiritual domains. The validated version of the Kessler scale was used to assess depressive symptoms. Linear regression analysis was performed to identify factors associated with the outcome variables, and a p-value < 0.05 with 95% CI was used to measure the degree of association between health-related quality of life and independent variables.

Results: The mean scores of health-related quality of life among HIV mono-infected patients in terms of thephysical, psychological, level of independence, social relationships, environmental, and spiritual health domains were 63.9, 65.0, 60.5, 59.0, 56.4, and 63.9, respectively; whereas the mean scores among TB/HIV co-infected patients were 46.6, 48.5, 42.7, 43.5, 39.3, and 51.3, respectively. Among HIV mono-infected patients, being married improved the quality of social relationships by 6.7 compared with unmarried patients (β = 6.7, 95% CI = 3.24, 10.11); whereas among the TB/HIV co-infected patients, being educated increased the quality of social relationships by 10.6 compared with being uneducated (β=10.6, 95% CI=3.70, 17.51).

Conclusion: The study revealed that the TB/HIV co-infected patients had poor health-related quality of life in all domains compared with HIV mono-infected patients. Besides, depression and stigma were more prevalent among co-infected patients. Therefore, designing and implementing specific management that focuses on psychiatric centers for TB/HIV co-infected patients will be necessary as their quality of life is lowered.

Keywords: health-related quality of life, HIV, tuberculosis, TB/HIV co-infection, Ethiopia

Correspondence: Lake Yazachew
University of Gondar, P. O. Box: 196, Gondar, Ethiopia
Email lyazachew07@gmail.com

Background

Tuberculosis (TB) is an infectious disease caused by the bacillus *Mycobacterium tuberculosis*. It is a primary cause of morbidity and mortality, and stands among the

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top-ranking causes of death globally. Transmission occurs when people inhale suspended bacteria in the environment that have been released in the breath of infected people.[1]

Worldwide, about 10 million people experienced TB illness in 2018. The incidence rate varies from country to country; it ranges from less than 5 to 500 new cases per 100,000 population, making the global average 130 on an annual basis.[1] Tuberculosis affects both sexes in all age groups but the highest burden is in men aged ≥15 years who accounted for 57% of all TB cases in 2018. Among all TB cases, 8.6% were people living with HIV (PLHIV).[1]

Tuberculosis is the most common opportunistic infection in PLHIV and it is the main cause of mortality among human immunodeficiency virus (HIV) patients. Worldwide, in 2017, 60% of notified TB patients had a documented HIV test result, up from 58% in 2016 and representing a 23-fold increase since 2004. In the World Health Organization (WHO) African region, where the burden of HIV-associated TB is highest, 86% of TB patients had a documented HIV test result. A total of 464,633 TB cases among HIV-positive people was reported; of these, 84.0% were on antiretroviral therapy (ART).[2]

HIV infection is a global public health concern which causes a chronic and debilitating disease. Since the first case of HIV was reported, more than 70 million individuals have been infected, and around 39 million people have died of HIV.[3]

The United Nations' call for reduction of tuberculosis mortality by three-fourths by 2020 among PLHIV is on the

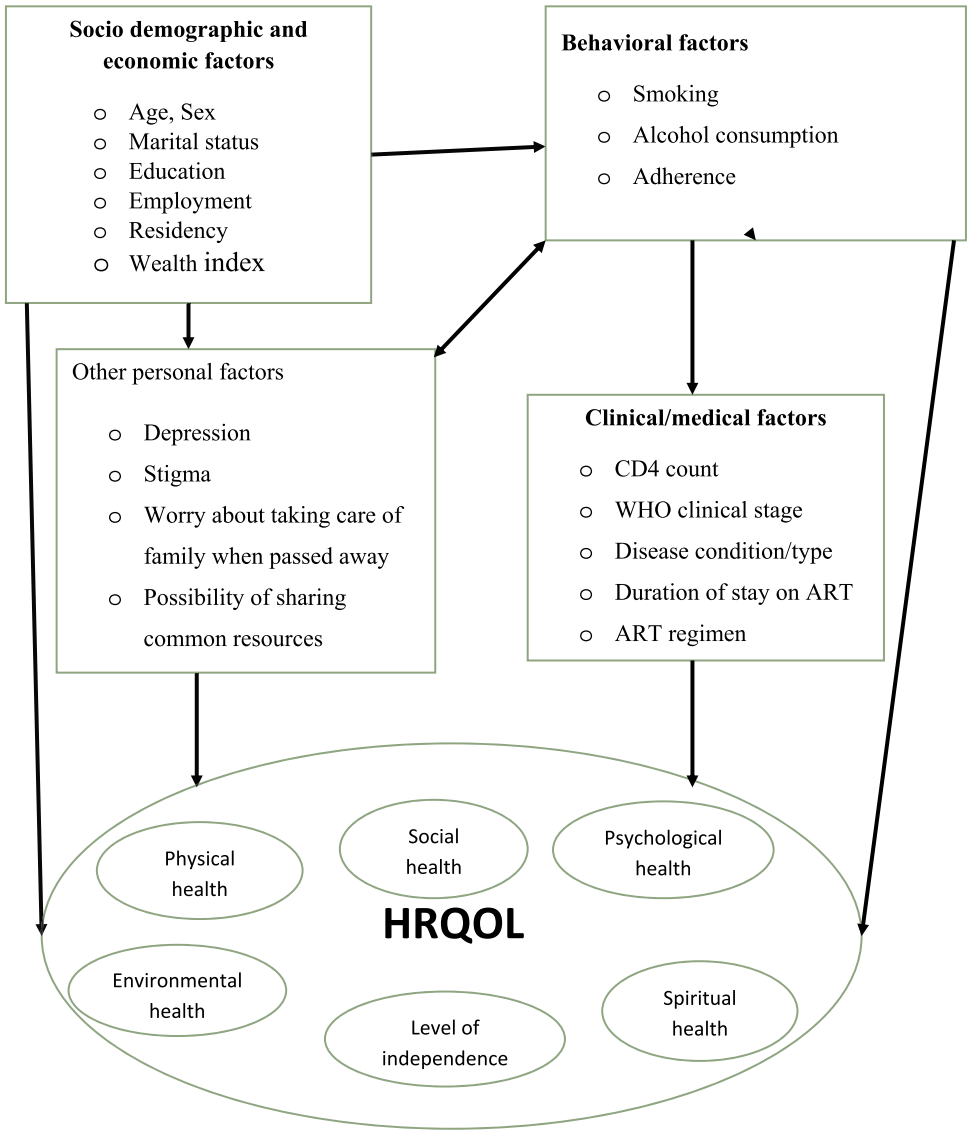

Figure 1 Conceptual framework for factors associated with HRQOL of HIV mono-infected and TB/HIV co-infected people from different literatures.[11,14–16,19–41]

way to being achieved. Among PLHIV, deaths attributed to TB dropped by more than two-fifths in the period 2010 to 2017.[4] However, there are some alarming concerns regarding PLHIV. In many countries a large number of PLHIV have still been dying from TB. Especially, the most vulnerable and marginalized groups have still been unable to access HIV and TB services. In PLHIV, the number of deaths due to TB has been rising in 40 countries around the world.[4,5]

In sub-Saharan Africa (SSA), women and girls continue to bear the effect of new HIV infection, accounting for three-fifths (59%) of all new HIV infections in the region in 2019. Though young women constituted only 10% of the SSA population, they accounted for 24% of new HIV infections in 2019, with 4500 young women becoming infected with HIV weekly.[5] People living with HIV are not only prone to the direct effect of the disease but also to stigma and depressive symptoms.[6,7]

Ethiopia is one of the most affected SSA countries with an estimated 729,089 PLHIV in 2018.[8] In Ethiopia, 0.9% of people aged 15–49 years are HIV positive, with a proportion of 1.2 and 0.6% among women and men, respectively.[9]

According to the WHO, quality of life (QOL) refers to individuals' psychological view of their surroundings in the perspective of the cultural, social and environmental context in which they live compared with their goals, outlooks, standards, and worries. QOL uses physical health, social relationships, environmental, level of independence, psychological, and spiritual components according to the WHO standard.[10]

In Brazil, at RibeirãoPreto-SP, an assessment of the QOL indicated that TB/HIV co-infected individuals presented lower mean scores than HIV mono-infected individuals in all areas, with important differences in the physical, psychological, level of independence and social relationships areas.[11]

In Ethiopia, the estimated number of TB incident cases among HIV patients was 16,000 in 2015, and the proportion of PLHIV with active TB in HIV care was 5.9%.[12] HIV mono-infected and TB/HIV co-infected individuals are faced with stigma, leading infected people to being rejected by their families, communities, and colleagues at their workplaces, and being seen as too weak for work. In addition, health workers' perception towards HIV mono-infected and TB/HIV co-infected patients could lead to mental stress, anxiety, and a reduction in health-related quality of life (HRQOL).[13] TB/HIV co-infected people experience stigma and/or misunderstanding, and tend to become isolated, and lose social support from persons significant to them;[14] these often affect their HRQOL.

Various evidences showed that socio-demographic, clinical, psychological and behavioral factors, immunological status, presence of symptoms, depression, stigma, and social support (Figure 1) are the most frequently and consistently reported factors associated with HRQOL among HIV mono-infected and TB/HIV co-infected people.[7,11,15–24] TB/HIV co-infection places a massive burden on health-care systems, particularly in highly affected countries such as Ethiopia.

The predominant aim of introducing highly active antiretroviral therapy (HAART) was to improve the wellbeing and QOL of affected people and it has led to a marked reduction in AIDS-related morbidity and mortality and changed the nature of the disease from deadly to chronically debilitating. With the appreciable rise in the longevity of people living with HIV and AIDS, it is essential to improve their QOL. Even though it is not clear how much impact HRQOL studies have on influencing the guidelines, published ART guidelines state that QOL must be considered in determining patient ARV regimens.[25] Though HIV mono-infected and TB/HIV co-infected people now live longer, their QOL usually harshly deteriorates. However, there is limited evidence in Ethiopia on how HIV mono-infected and TB/HIV co-infected people perceive their HRQOL.

Therefore, this study was conducted to assess the level of HRQOL and associated factors among HIV and TB/HIV co-infected adult patients in the public health facilities of Dessie town, northeast Ethiopia. This could help to design a better management system for those patients in order to improve their HRQOL.

Methods

Study Design and Settings

A comparative facility-based cross-sectional study was conducted in public health facilities of Dessie town, northeast Ethiopia from February 01 to May 30, 2019. Dessie town is the capital city of South Wollo zone, which is located 401 kilometers to the north of Addis Ababa, the capital city of Ethiopia. The town consists of one referral and one general public hospital, and eight health centers which provide curative, preventive, rehabilitative, and other services for an estimated population of 150,174. During the study period, there were 10,430 HIV mono-

infected and 315 TB/HIV co-infected patients registered with the public health facilities of Dessie town.

Population and Sampling

All adult HIV mono-infected and TB/HIV co-infected patients who visited the public health facilities of Dessie town were the source population whereas all adult HIV mono-infected and TB/HIV co-infected patients who visited the public health facilities of Dessie town during the data collection period were the study population. All adult HIV mono-infected people who were 18 years and above with or without TB co-infection and who were receiving antiretroviral drugs for at least one month before the start of data collection were included in the study. We took one month as the cut-off point for inclusion, to prevent underestimation of QOL due to ART initiation, which results in immune reconstitution syndrome in the first month. Pregnant women, patients who were defaulters, patients who began treatment after failure, and relapse cases for TB treatment among the co-infected and patients with other co-morbidities were excluded.

The sample size of the study was calculated considering a previous study done in Ethiopia,[16] through a power approach. It was determined using STATA 14 software by taking the standard deviation and mean value of each domain which was found to be significant for HIV mono-infected and TB/HIV co-infected patients, considering confidence level at 95%, power 80%, ratio of 1:3 (TB/HIV to HIV), and adding 10% non-response rate. Therefore, the sample size, 612 (459 HIV and 153 TB/HIV co-infected patients), determined for the environmental domain of HRQOL was taken as the final sample size as this was greater than the sample size determined for other domains of HRQOL.

Among all the health facilities in Dessie town, five health facilities were ART sites from which HIV mono-infected patients were selected. The TB/HIV co-infected patients were selected from all public health facilities which were providing Directly Observed Short Course Therapy (DOTs). The sample was allocated proportionally across the health facilities based on their number of patients on follow-up. The HIV mono-infected and TB/HIV co-infected patients were selected by a simple random sampling method using their respective lists as a sampling frame from the ART clinic and TB unit.

Variables and Measurement

The domains of the HRQOL (physical, psychological, social relationships, independence level, environmental, and spiritual) among adult HIV mono-infected and TB/HIV co-infected people were the dependent variables. Socio-demographic and economic factors, behavioral factors, clinical/medical characteristics, and other personal factors were the independent variables of the study.

The HRQOL is a multi-dimensional construct which refers to patients' perception of the impact of disease and treatment on their physical, psychological, social, independence, environmental, and spiritual aspects where the means of each WHOQOL-HIV BREF domain score were the dependent variables.[7,26,27] The HRQOL was measured using the six domains with a total of 31 items that include 4 items of physical, 5 items of psychological, 4 items of social relationships, 8 items of environmental, 4 items of level of independence, and 4 items of spiritual domains of the HRQOL, and 2 items/questions of general QOL and perceived general health. Each item/question had a five-point Likert scale where 1 indicated low or negative perceptions and 5 indicated high or positive perceptions. Negatively framed/asked question items were transformed to positive responses for ease of computations. Raw and transformed scores were done for the outcome variable using the means of domains and multiplied by 4 for comparison with the WHO standard. Finally, the transformed value of each domain was calculated and changed to 100 by using the formula;

$$Transformed\ scale = \frac{(domain\ score - minimum\ possible\ domain\ score)}{domain\ score\ range} * 100$$

Smoking status was measured by using WHO guidelines for controlling and monitoring the tobacco epidemic and categorized as smoker and non-smoker.[28] A smoker is a person who, smokes any tobacco product either daily or occasionally i.e., smokers can be individuals who smoke either daily or occasionally during the study period. A non-smoker is a person who does not smoke at all during the study period. Non-smokers can be ex-smokers, never-smokers, or ex-occasional smokers.

Alcohol consumption was assessed using the FAST alcohol screening test measurement scale, which has 4 questions and 5-point Likert scales. For questions 1, 2 and 3, we used 0–4 Likert scales of 0–4 (0 = never, 1 = Less than monthly, 2 = monthly, 3 = weekly, 4 = daily or almost daily). However, for question 4 we used 0 for No, 2 for Yes (on one occasion), and 3 for Yes (on more than one occasion) and categorized itinto two categories. The minimum score was 0, and the maximum score was 16. The

score for hazardous drinking was 3 or more, and categorized into two categories: a score of < 3 was labelled as non-hazardous drinkers, and a score of ≥ 3 was labelled as hazardous drinkers.[29]

Wealth status was measured using 13 items for urban, and 10 for rural residents. A principal component analysis (PCA) was also done to compute the wealth index by taking variables with eigenvalue greater than one after checking their correlation matrix and commonalities. Finally, wealth status was ranked into three categories: low, middle, and high.[30, 31]

Depression was assessed by the Kessler-6 scale,[7,32,33] which consists of six questions with a 5-point Likert scale (1= none, 2= a little, 3= some, 4= most, and 5= all). It was categorized into two: "not depressive" if the score was below the mean (the mean score was 12), and "depressive" if it was above the mean. Stigma was measured with the 6-item Internalized AIDS-Related Stigma Scale (IA-RSS),[34,35] containing a dichotomous response scale of "agree" or "disagree." Scale scores were summed to obtain composite stigma scores ranging from 0 to 6, and finally, those who scored below the mean (mean was 3) were labeled as "not stigmatized" and above the mean were labeled as "stigmatized."

The internal consistency of the WHOQOL-HIV-BREF instrument was assessed through the Cronbach's alpha value estimation. The Cronbach's alpha reliability coefficient of the overall WHOQOL-HIV-BREF, and physical, psychological, level of independence, social relationships, environmental, and spiritual domains of HRQOL were 0.83, 0.53, 0.69, 0.65, 0.67, 0.75, and 0.58, respectively

Data Collection Tools and Procedure

An interviewer-administered structured questionnaire was adapted for data collection after reviewing relevant studies.[7,29–36] The questionnaire was first prepared in English, then translated to the local language (Amharic) and was back-translated to English to check its consistency. Face to face interview was employed using the short Amharic version of the World Health Organization Quality of Life Instrument for HIV clients (WHOQOL-HIV-BREF). Private space was prepared for data collection, and the interview took on average 31 minutes per participant. This instrument was validated and used previously in Ethiopia.[16,37]

Training was given for data collectors and supervisors. The supervisors made close supervision while the principal investigator monitored and facilitated the overall process of data collection. A pretest was conducted on 24 HIV mono-infected and five TB/HIV co-infected patients (5% of the total sample) at Kobo primary hospital and Kobo health center, and necessary corrections and amendments were made on the tool before the actual data collection. Furthermore, during data collection, supervisors checked the data for accuracy, consistency, and completeness on a daily basis.

Data Processing and Analysis

The collected data were cleaned, coded, and entered into Epi-Data version 3.1 and exported to STATA version 14 for analysis. Descriptive statistics such as mean and standard deviation were used to describe the data. Linear regression was performed to identify factors associated with the outcome variable after checking model assumptions such as normality, equal variance, multicollinearity, and linearity. The F-test was also used to see the model fitness. Variables which had significant association with the outcome variable at a p-value of less than or equal to 0.2 in the simple regression analysis were considered as candidate variables for the final model, multiple linear regression. In the final multiple linear regression model, a p-value of less than 0.05 with 95% CI was used to declare significance of variables with the outcome variables.

Results

Socio-Demographic, Personal, Behavioral, and Medical Characteristics of Participants

A total of 434 HIV mono-infected and 143 TB/HIV co-infected patients participated in the study with a response rate of 94.3%. The mean age of the HIV mono-infected and TB/HIV co-infected patients was 37.27±8.86 and 36.27±7.44 years, respectively. Nearly 62% and 55% of the HIV mono-infected, and TB/HIV co-infected patients were female, respectively. The median duration of treatment on ART was 74 months (with IQR of 72 months) in HIV mono-infected patients and 85 months (with IQR of 72 months) in TB/HIV co-infected patients. The median value of CD4 count was 463 (with IQR of 300) in the HIV mono-infected patients, and 360 (with IQR of 183) in TB/HIV patients. Table 1

Table 1 Sociodemographic, Personal, Behavioral and Medical Characteristics of the Study Population Northeast Ethiopia, 2019

Variables	HIV (n=434)	TB/HIV (n=143)
	n (%)	n (%)
Sociodemographic characteristics		
Type of facility		
Specialized hospital	197 (45.40)	49 (34.27)
General hospital	94 (21.65)	26 (18.18)
Health center	143 (32.95)	68 (47.55)
Age in years, Mean (SD)	37.27 (8.86)	36.27 (7.44)
Sex		
Female	267 (61.52)	79 (55.24)
Male	167 (38.48)	64 (44.76)
Marital status		
Married	249 (57.37)	84 (58.74)
Unmarried	185 (42.63)	59 (41.26)
Religion		
Muslim	228 (52.53)	68 (47.55)
Christian	206 (47.47)	75 (52.45)
Occupational status		
Employed	137 (31.57)	58 (40.56)
Unemployed	120 (27.65)	37 (25.87)
Merchant	78 (17.97)	14 (9.79)
Daily laborer	60 (13.82)	17 (11.89)
Farmer	39 (8.99)	17 (11.89)
Residence		
Urban	374 (86.18)	118 (82.52)
Rural	60 (13.82)	25 (17.48)
Educational status		
Uneducated	109 (25.12)	40 (27.97)
Primary	115 (26.50)	36 (25.17)
Secondary	144 (33.18)	46 (32.17)
Higher	66 (15.21)	21 (14.69)
Ethnicity		
Amhara	414 (95.39)	132 (92.31)
Tigre	13 (3.00)	4 (2.80)
Oromo	6 (1.38)	6 (4.20)
Other	1 (0.23)	1 (0.70)
Wealth index		
Low	144 (33.18)	58 (40.56)
Moderate	148 (34.10)	34 (23.78)
High	142 (32.72)	51 (35.66)
Personal characteristics		
PSCR		
Not at all	159 (36.64)	63 (44.06)
A little	70 (16.13)	26 (18.18)
Moderately	157 (36.18)	46 (32.17)
Very much	48 (11.06)	8 (5.59)
EWTF		
Not at all	151 (34.79)	46 (32.17)
A little	99 (22.81)	24 (16.78)
Moderately	112 (25.81)	47 (32.87)
Very much	72 (16.59)	26 (18.18)
Depression status		
Depressive	36 (8.29)	60 (41.96)
Not depressive	398 (91.71)	83 (58.04)
Stigma scale		
Stigmatized	180 (41.47)	84 (58.74)
Not stigmatized	254 (58.53)	59 (41.26)
Behavioral characteristics		
Alcohol intake		
Hazardous drinker	153 (35.25)	43 (30.07)
Non-hazardous drinker	281 (64.75)	100 (69.93)
Smoking status		
Smoker	16 (3.69)	8 (5.59)
Nonsmoker	418 (96.31)	135 (94.41)
Medical characteristics		
Duration since the disease diagnosed in months		
Median (IQR)	74 (72)	85 (72)
WHO clinical stage		
Stage I	386 (88.94)	NA
Stage II	42 (9.68)	NA
Stage III	6 (1.38)	98 (68.53)
Stage IV	NA	45 (31.47)
CD4 count		
Median (IQR)	463 (300)	360 (183)
Types of TB disease		
HIV/SMEAR +VE PTB	NA	69 (48.25)
HIV/EPTB		30 (20.98)
HIV/MDR TB		23 (16.08)
HIV/SMEAR -VE PTB		19 (13.29)
HIV/XDR TB		2 (1.40)
Type of ART drug that the participant took		
1C	79 (18.20)	25 (17.48)
1D	63 (14.52)	19 (13.29)
1E	226 (52.07)	87 (60.84)
1F	64 (14.75)	5 (3.50)
OTHER	2 (0.46)	7 (4.90)

Abbreviations: PSCR, possibility of sharing common resources with other people; EWTF, extent to which worry about taking care of the family when passed away; 1C, AZT-3TC-NVP; 1D, AZT-3TC-EFV; 1E, TDF-3TC-EFV; 1F, TDF-3TC-NVP; NA, not applicable.

Health-Related Quality of Life of Patients

The mean scores of HRQOL among HIV mono-infected patients in terms of the physical, psychological, level of independence, social relationships, environmental, and spiritual health domains of HRQOL were 63.9, 65.0, 60.5, 59.0, 56.4, and 63.9, respectively whereas the mean scores for physical health, psychological, level of independence, social relationships, environmental, and spiritual domains of the HRQOL among TB/HIV co-infected patients were 46.59, 48.53, 42.65, 43.53, 39.31, and 51.26, respectively. In most HRQOL domains, depressive symptoms score was higher in TB/HIV co-infected patients (mean ± SD=10.3±5.18) than HIV mono-infected patients (mean± SD = 5±4.18) at a p-value of 0.001. Similarly, stigma score was higher in TB/HIV co-infected patients (mean ± SD=3.33±2.18) than HIV mono-infected patients (mean ± SD= 2.47±1.95) at a p-value of 0.001. All HRQOL domain scores in TB/HIV co-infected patients were less than the scores in the HIV mono-infected patients. Table 2

Factors Associated with the Health-Related Quality of Life

Physical Domain of the HRQOL of Patients

The study revealed that occupational status, educational status, the possibility of sharing common resources with other people, wealth status, and depression in HIV mono-infected patients; and educational status and the possibility of sharing common resources with other people in TB/HIV co-infected patients were variables significantly associated with the physical domain of HRQOL.

The study showed that HIV mono-infected patients who were employed, who were educated, who had a moderate possibility of sharing common resources, and who had high-income status had an increased physical domain of the HRQOL by 4.3 (β = 4.3; 95% CI: 0.68, 7.91), 4.6 (β = 4.6; 95% CI: 0.54, 8.58), 5.1 (β = 5.14; 95% CI: 1.50, 8.77), and 5.3 (β = 5.29; 95% CI: 1.54, 9.05) compared with patients who were unemployed, who were uneducated, who had no possibility of sharing common resources, and who had low-income status, respectively. HIV mono-infected patients who were depressed had a decreased physical domain of HRQOL by 8.9 (β = −8.92; 95% CI: −14.9, −3.16) compared with those who were not depressed.

The TB/HIV co-infected patients who were educated and who had a little possibility of sharing common resources had an increased physical domain of HRQOL by 7.72 (β = 7.72; 95% CI: 1.20, 14.23) and 8.91 (β = 8.91; 95% CI: 1.23 16.59) compared with patients who were uneducated, and who had no possibility of sharing common resources at all, respectively. Table 3

Table 2 Comparison Between Domains of Health-Related Quality of Life of TB/HIV and HIV Patients, Northeast Ethiopia, 2019

Quality of Life Domains	TB/HIV (n=143) Mean (±SD)	HIV (n=434) Mean (±SD)	p-value
Physical domain	46.59 (16.81)	63.9 (16.99)	0.001
Psychological domain	48.53 (15.46)	65 (15.45)	0.001
Level of independence	42.65 (19.61)	60.5 (17.89)	0.001
Social relation	43.53 (18.73)	59 (18.51)	0.001
Environmental domain	39.31 (14.23)	56.4 (14.08)	0.001
Spiritual domain	51.26 (20.17)	63.9 (20.37)	0.001
Depressive symptoms	10.34 (5.18)	5.5 (4.18)	0.001
Stigma score	3.33 (2.18)	2.47 (1.95)	0.001

Psychological Domain of the HRQOL of Patients

The study revealed that age, educational status, wealth status, and depression in HIV mono-infected patients, and stigma in HIV/TB co-infected patients, were factors significantly associated with the psychological domain of HRQOL.

The HIV mono-infected patients whose age was greater than 35 years, who were educated, and who had high-income status had an increased psychological domain of HRQOL by 4.3 (β = 4.3; 95% CI: 1.39, 7.14) 5.6 (β = 5.61; 95% CI: 1.97, 9.25) and 3.5 (β = 3.52; 95% CI: 0.17, 6.88) compared with patients whose age was less than or equal to 35 years, who were uneducated, and who had low-income status, respectively. However, depressed HIV mono-infected patients had a decreased psychological domain of HRQOL by 12 (β = −12; 95% CI: −16.84, −6.68) compared with those who were not depressed.

Besides, stigmatized TB/HIV co-infected patients had a decreased psychological domain of HRQOL by 5.8 (β = −5.78; 95% CI: −11.31, −0.25) compared with non-stigmatized patients. Table 3

Level of Independence Domain of the HRQOL of Patients

The study revealed that sex, educational status, and wealth status in HIV mono-infected patients, and residence and wealth status in TB/HIV co-infected patients, were variables significantly associated with the level of independence domain of HRQOL.

Table 3 Factors Associated with the Physical and Psychological Domains of the HRQOL in HIV Mono-Infected and TB/HIV Co-Infected Patients in Public Health Facilities, Northeast Ethiopia, 2019

Variables	Category	Domains			
		Physical Domain		Psychological Domain	
		HIV (n=434)	TB/HIV (n=143)	HIV (n=434)	TB/HIV (n=143)
		B (95% CI)	β (95% CI)	B (95% CI)	B (95% CI)
Age (mean =35)	>35	NA	−1.34 (−7.40, 4.72)	4.3 (1.39, 7.14) *	NA
Sex	Female	−1.8 (−5.15, 1.63)	NA	−2.56 (−5.59, 0.47)	−3.83 (−9.19, 1.54)
Marital status	Married	2.45 (−0.72, 5.62)	NA	1.86 (−0.88, 4.61)	3.50 (−1.87, 8.86)
Occupational status	Employed	4.30 (0.68, 7.91) *	NA	1.8 (−1.38, 4.50)	NA
Residence	Urban	2.16 (−2.80, 7.11)	NA	1.8 (−2.67, 6.18)	NA
Educational status	Educated	4.56 (0.54, 8.58)*	7.72 (1.20, 14.23) *	5.61 (1.97, 9.25) *	4.43 (−1.50, 10.36)
PSCR	Not at all	0	0	NA	0
	A little	3.18 (−1.49, 7.85)	8.91 (1.23, 16.59) *		5.97 (−1.30, 13.24)
	Moderately	5.14 (1.50, 8.77) *	1.97 (−4.35, 8.30)		0.44 (−5.71, 6.59)
	Very much	−0.90 (−6.45, 4.65)	0.18 (−12.09, 12.45)		−3.30 (−14.93, 8.33)
EWTF	Not at all	3.66 (−1.18, 8.50)		NA	−4.83 (−12.62, 2.96)
	A little	1.47 (−3.72, 6.67)	NA		−2.77 (−11.10, 5.56)
	Moderately	1.65 (−3.36, 6.67)			−1.40 (−8.98, 6.19)
	Very much	0			0
Duration (median=80)	>80	NA	NA	0.05 (−2.83, 2.93)	−3.32 (−8.43, 1.78)
WHO stage	I	11 (−2.23, 24.27)		−0.5 (−12, 11)	
	II	11 (−3.17, 24.83)	NA	3.6 (−8.54, 15.77)	NA
	III	0		0	
	IV	NA		NA	
Depression symptoms	Depressive	−8.9 (−14.64, −3.20) *	−3.73 (−9.39, 1.93)	−12 (−16.84, −6.68)*	−3.53 (−8.82, 1.77)
Stigma scale	Stigmatized	−2.69 (−5.88, 0.50)	−1.70 (−7.68, 4.28)	NA	−5.78 (−11.31, −0.25) *
Alcohol intake	HAD	0.87 (−2.79, 4.54)	NA	−1.99 (−5.23, 1.25)	NA
Smoking status	Smoker	−5.6 (−14.1, 2.87)	NA	NA	NA
Wealth index	Low	0	0	0	0
	Middle	3.50 (−0.23, 7.23)	−0.56 (−7.57, 6.46)	0.21 (−3.14, 3.57)	0.71 (−5.87, 7.28)
	High	5.29 (1.53, 9.05) *	4.13 (−2.85, 11.11)	3.52 (0.17, 6.88)*	2.92 (−3.34, 9.17)
Adjusted R^2		0.1642	0.1065	0.1811	0.1096

Note: *Statistically significant value at $p < 0.05$.

Abbreviations: NA, not applicable; PSCR, possibility of sharing common resources; EWTF, extent to which worry about taking care of family when passed away; HAD, hazardous alcohol drinker.

The HIV co-infected patients who were educated, and who had high-income status had an increased level of independence domain of HRQOL by 4.8 (β = 4.86; 95% CI: 1.08, 8.63) and 9.1 (β = 9.11, 95% CI: 5.11, 13.11) compared with patients who were uneducated and who had low-income status, respectively. However, female HIV mono-infected patients had a decreased level of independence domain of HRQOL by 5.5 (β = −5.48; 95% CI: −8.96, −2.00) compared with male patients.

The TB/HIV co-infected patients who had high-income status had an increased level of independence domain of HRQOL by 10.4 (β =10.41; 95% CI: 2.00, 18.8) compared with participants with low-income status whereas TB/HIV co-infected patients who were urban residents had a decreased level of independence domain of HRQOL by 9.4 (β = −9.43, 95% CI: −18.40, −0.46) compared with rural residents. Table 4

Social Domain of the HRQOL of Patients

The study indicated that marital status, educational status, wealth status, depression, and stigma, in HIV mono-

Table 4 Factors Associated with the Level of Independence and Social Relation Domains of the HRQOL in HIV Mono-Infected and TB/HIV Co-Infected Patients in Public Health Facilities, Northeast Ethiopia, 2019

Variables	Category	Domains			
		Level of Independence Domain		Social Relation Domain	
		HIV (n=434)	TB/HIV (n=143)	HIV (n=434)	TB/HIV (n=143)
		β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Sex	Female	−5.48 (−8.96, −1.99) *	−2.52 (−9.08, 4.04)	−1.28 (−4.84, 2.27)	0.33 (−5.98, 6.65)
Marital status	Married	2.47 (−0.88, 5.82)	−3.42 (−10.06, 3.21)	6.67 (3.24, 10.11) *	3.21 (−2.79, 9.21)
Occupational status	Employed	2.00 (−1.81, 5.80)	NA	0.87 (−3.01, 4.75)	NA
Residence	Urban	NA	−9.43 (−18.40, −0.46) *	NA	7.63 (−0.87, 16.13)
Educational status	Educated	4.86 (1.08, 8.63) *	NA	3.93 (0.08, 7.78) *	10.6 (3.70, 17.51) *
EWTF	Not at all	3.22 (−1.65, 8.10)		4.50 (−0.48, 9.47)	
	A little	4.35 (−0.88, 9.58)		4.26 (−1.08, 9.59)	
	Moderately	1.48 (−3.52, 6.48)	NA	2.99 (−2.11, 8.08)	NA
	Very much	0		0	
CD4 count (median=439)	>439	NA	−4.41 (−11.45, 2.63)	NA	0.62 (−5.98, 7.21)
Depression symptoms	Depressive	−4.27 (−10.28, 1.73)	−4.77 (−11.43, 1.88)	−12.8 (−18.96, −6.64) *	−10 (−16.3, −4.39) *
Stigma scale	Stigmatized	NA	−0.38 (−7.14, 6.39)	−5.14 (−8.62, −1.66) *	NA
Smoking status	Smoker	NA	NA	NA	4.7 (−8.47,17.84)
Wealth index	Low	0	0	0	0
	Middle	3.93 (−0.02, 7.88)	2.60 (−5.58,10.77)	2.64 (−1.40, 6.68)	0.24 (−7.21,7.69)
	High	9.11 (5.11, 13.11) *	10.41 (2.00, 18.8) *	4.92 (0.84, 9.01) *	9.04 (1.52, 16.55)*
Adjusted R^2		0.1263	0.1305	0.1429	0.1760

Note: *Statistically significant value at $p < 0.05$.
Abbreviations: NA, not applicable; EWTF, extent to which worry about taking care of family when passed away.

infected patients; and educational status, wealth status, and depression in TB/HIV co-infected patients were variables significantly associated with the social relationships domain of the HRQOL.

The HIV mono-infected patients who were married, who were educated, and who had high-income status had an improved social domain of HRQOL by 6.7 (β = 6.7; 95% CI: 3.24, 10.11), 3.9 (β = 3.93; 95% CI: 0.08, 7.78), and 4.9 (β = 4.92; 95% CI: 0.84, 9.01) compared with patients who were unmarried, who were uneducated, and who had low-income status, respectively. Depressed and stigmatized HIV mono-infected patients had a lower social domain of HRQOL by 12.8 (β = −12.8; 95% CI: −18.96, −6.64), and 5.1 (β = −5.14; 95% CI: −8.62, −1.66) compared with patients who were not depressed and who were not stigmatized, respectively.

The TB/HIV co-infected patients who were educated, and who had high-income status had an increased social domain of HRQOL by 10.6 (β = 10.6; 95% CI: 3.70, 17.51) and 9.04 (β = 9.04; 95% CI: 1.52, 16.55) compared with patients who were uneducated, and who had low-income status, whereas TB/HIV co-infected patients who were depressed had a decreased social domain of HRQOL by 10.4 (β= −10.4, 95% CI= −16.31, −4.39) compared with patients who were not depressed. Table 4

Environmental Domain of the HRQOL of Patients

The study showed that residence, educational status, worrying about the family if one passes away due to the disease, depression, stigma, and wealth status in HIV mono-infected patients; and educational status, depression, stigma, and wealth status in TB/HIV co-infected patients were variables significantly associated with the environmental domain of the HRQOL.

The study showed that HIV mono-infected patients who were urban residents, who were educated, who were not worrying at all or were worrying a little, and who had middle- and high-income status had an increased environmental domain of HRQOL by 4.99 (β = 4.99; 95% CI: 1.24, 8.75), 4.6 (β = 4.6; 95% CI: 1.59, 7.63), 7.2 (β = 7.24; 95% CI: 3.83, 10.64) and 6.6 (β = 6.6; 95% CI: 2.88,

10.31), and 4.2 (β = 4.19; 95% CI: 1.35, 7.02) and 10.4 (β = 10.4; 95% CI: 7.56, 13.26) compared with patients who were rural residents, who were uneducated, who were worrying about their family if they were to pass away due to the disease, and who had low-income, respectively. Conversely, depressed and stigmatized HIV mono-infected patients had a decreased environmental domain of HRQOL by 10.2 (β = −10.2; 95% CI: −14.48, −5.94) and 2.5 (β = −2.55; 95% CI: −4.98, −0.13) compared with patients who were not depressed and not stigmatized, respectively.

The TB/HIV co-infected patients who were educated, and who had high-income status had an increased environmental domain of HRQOL by 9.3 (β = 9.29; 95% CI: 4.08, 14.49) and 12.1 (β = 12.12, 95% CI: 6.88, 17.36) compared with patients who were uneducated, and who had a low-income, respectively. Conversely, depressed and stigmatized TB/HIV co-infected patients had a lower environmental domain of HRQOL by 4.4 (β = −4.39; 95% CI: −8.71, −0.06) and 5.09 (β = −5.09; 95% CI: −9.56, −0.63) compared with participants who were not depressed, and who were not depressed, respectively. Table 5

Spiritual Domain of the HRQOL of Patients

The study indicated that duration of treatment on ART, WHO clinical stage of HIV, depression, and stigma in HIV mono-infected patients; and wealth status and WHO clinical stage of HIV in TB/HIV co-infected patients were factors significantly associated with the spiritual domain of the HRQOL.

The HIV mono-infected patients who had stayed on ART treatment for a median duration of more than 80 months, and who were at WHO stage I and II had an increased spiritual domain of HRQOL by 5.2 (β = 5.16; 95% CI: 1.47, 8.85), and 25.5 (β = 25.5; 95% CI: 10.59, 40.41) and 34.2 (β = 34.2; 95% CI: 18.28, 50.13) compared with patients who stayed on treatment for less than or equal to 80 months, and who were at WHO stage III, respectively. However, depressed and stigmatized HIV mono-infected patients had a decreased spiritual domain of HRQOL by 6.98 (β = −6.98; 95% CI: −13.35, −0.62) and 11.4 (β = −11.4: 95% CI: −14.99, −7.66) compared with patients who were not depressed and stigmatized, respectively.

The TB/HIV co-infected patients who were categorized under middle-income status and who were at WHO stage III had an increased spiritual domain of HRQOL by 9.77 (β = 9.77; 95% CI: 0.87, 18.68) and 10.9 (β = 10.9: 95% CI: 0.41, 21.29) compared with patients who had low-income status, and who were at WHO stage IV, respectively. Table 5

Discussion

The study indicated that age, sex, marital status, occupational status, educational status, and residence of the study participants were significantly associated with the HRQOL of patients.

The findings showed that the HRQOL scores of the TB/HIV co-infected patients were low in all domains compared with those of HIV mono-infected patients. The reason for this might be that TB co-infection aggravates the symptoms of HIV and facilitates the progression of HIV to the advanced stage, complicates the disease management and adds burden on the individuals.[38] Even though this might not be a perfect comparison, the finding is supported by a study conducted in Ethiopia that shows HIV/Visceral Leishmaniasis co-infected people have a poorer HRQOL in all domains than HIV infected people.[27] Moreover, this finding is comparable with the studies conducted in Brazil, Nigeria, and Ethiopia.[11,16,22,39] The possible explanation might be that since TB is a contagious disease people might decrease their interaction with others to minimize the transmission.

In most HRQOL domains, depressive symptoms score was higher in TB/HIV co-infected patients than HIV mono-infected patients. Similarly, stigma score was higher in TB/HIV co-infected patients than HIV mono-infected patients. The finding is in line with the study conducted in Nepal and Ethiopia.[7,16,17,20] The possible explanation might be because the additional disease (TB) makes PLHIV become more depressed and stigmatized due to the nature of its infectiousness.[40]

The study revealed that age of the patients was significantly associated with the psychological domain of the HRQOL of the HIV mono-infected patients where older age signified better psychological health. This is in line with a study conducted in India[21] which suggests old age has a positive relation with QOL. However, this finding is inconsistent with other studies conducted in Bangladesh and Vietnam,[41] China,[42] and Canada[43] which show older age has an inverse relation with the HRQOL. The possible explanations for this might be the difference in methods used to measure this HRQOL and the difference in the socio-demographic characteristics of the study participants.

Table 5 Factors Associated with the Environmental and Spiritual Domains of the HRQoL in HIV Mono-Infected and TB/HIV Co-Infected Patients in Public Health Facilities, Northeast Ethiopia, 2019

Variables	Category	Domains			
		Environmental Domain		Spiritual Domain	
		HIV (n=434)	TB/HIV (n=143)	HIV (n=434)	TB/HIV (n=143)
		β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Age (mean= 35)	>35	NA	−0.51 (−5.19, 4.18)	2.10 (−1.44, 5.64)	NA
Sex	Female	NA	0.18 (−4.36, 4.72)	NA	−5.3 (−12.17,1.59)
Residence	Urban	4.99 (1.24, 8.75) *	NA	NA	NA
Educational status	Educated	4.61 (1.59, 7.63)*	9.29 (4.08, 14.49) *	NA	NA
Possibility of sharing common resources	Not at all A little Moderately Very much	NA	0 0.27 (−5.56, 6.10) −4.70 (−9.46, 0.05) −6.95 (−16.22, 2.32)	0 0.16 (−5.04, 5.35) 1.37 (−2.70, 5.45) 1.77 (−4.26, 7.79)	NA
Worrying about the family if one passes away due to the disease	Not at all A little Moderately Very much	7.24 (3.83, 10.64) * 6.60 (2.88, 10.31) * 2.36 (−1.20, 5.92) 0	NA	NA	NA
Duration (Median=80)	>80	NA	−2.45 (−6.63, 1.73)	5.16 (1.47, 8.85) *	NA
WHO stage	I II III IV	NA	NA	25.5 (10.59, 40.41) * 34.2 (18.28, 50.13) * 0 NA	NA NA 10.9 (0.41, 21.29)* 0
CD4 count (median=439)	>439	NA	−0.75 (−5.39, 3.88)	NA	NA
Depression symptoms	Depressive	−10.2 (−14.48, −5.94) *	−4.39 (−8.71, −0.06) *	−6.98 (−13.35, −0.62) *	−5.8 (−12.5, 0.90)
Stigma scale	Stigmatized	−2.55 (−4.98, −0.13) *	−5.09 (−9.56, −0.63) *	−11.4 (−14.99, −7.66) *	NA
Alcohol intake	HAD	NA	NA	−1.43 (−5.58, 2.73)	NA
Smoking status	Smoker	NA	−4.51 (−4.71, 13.73)	0.44 (−8.87, 9.75)	NA
Wealth index	Low Middle High	0 4.19 (1.35, 7.02) * 10.4 (7.56, 13.26) *	0 5.21 (−0.01, 10.43) 12.12 (6.8, 17.36) *	0 −0.46 (−4.68, 3.76) −3.19 (−7.39, 1.01)	0 9.77 (0.87, 18.68)* 1.99 (−5.79, 9.78)
Adjusted R^2		0.287	0.307	0.2300	0.0779

Note: *Statistically significant value at $p < 0.05$.
Abbreviations: NA, not applicable; HAD, hazardous alcohol drinker.

In this study, being female was associated with lower independence levels compared with males in the mono-infected group, and this is consistent with the finding from a study done in the United States of America[44,45] and Ethiopia.[19,23,46] The possible reason for this might be that females are overburdened with household activities and raising children which could make them weaker, and decrease their work capacity.

The study revealed that being married resulted in an improved social relationships domain compared with unmarried participants. This is in line with the finding of a study conducted on the psychosocial impact and QOL of people with HIV/AIDS in south India[47] in which being married had a positive relationship with the social relationships domain of QOL. However, it is in contrast with the findings of other studies conducted in Ethiopia and India[7,21] in which being married resulted in lower QOL scores in all domains of the HRQOL compared with single and unmarried people. This could be due to the stress and fear which might be higher in the previous studies among

married partners that resulted from blaming each other for being HIV positive.

The study revealed that being employed had a positive relationship with the physical domain of the HRQOL among HIV mono-infected patients. This is similar to the findings from studies conducted in Ethiopia,[23] Canada,[48] and a study conducted on the socioeconomic factors and HRQOL of adult HIV mono-infected people.[49] The result may be attributable to being employed which enables people to feel good, strong, confident, and self-sufficient and hence could result in better HRQOL.

In this study, educational status was significantly associated with the physical, social, and environmental domains of the HRQOL of both HIV mono-infected and TB/HIV co-infected patients. Besides, it was significantly associated with psychological and independence level domains of the HRQOL of HIV mono-infected patients. This finding is consistent with studies conducted in Ethiopia and Nepal[20,22] which show that being educated has a significant association with improved QOL in most of the domains. The possible reason for this may be that education increases the possibility of having a job, accessing technologies, and making life relatively favorable and easy.

The study also indicated that being urban dwellers had a negative relationship with the level of independence domain of the HRQOL in TB/HIV co-infected patients while it had a positive relationship with the environmental health domain of the HRQOL in HIV mono-infected patients. The positive relationship of being urban dwellers with the environmental health domain is in line with the finding of the study conducted in Ethiopia. However, the positive relationship of being urban dwellers with the level of the independence domain is in contrast with the finding of the same study.[22] This difference might be because in a rural community there is a small difference regarding the social classes and a minimum gap between the high class and lower class in respect to living standards compared with urban residents, whereas the possible reason for the positive relationship between urban residency and environmental health might be due to the fact that in urban areas getting the needed infrastructures and means of transportation is relatively easier than for rural residents.

Sharing common resources with other people was found to have a positive significant association with the physical domain of HRQOL in both HIV mono-infected and HIV/TB co-infected patients. The finding is inconsistent with the result of a study conducted in Ethiopia[7] in which there was no significant relationship between sharing common resources and the physical domain of HRQOL.

Worrying about their family situation if they pass away due to the disease had a negative significant association with the environmental domain of the HRQOL in the HIV mono-infected patients. This might be due to the lack of financial security the family will face. This finding confirms a research finding from Ethiopia.[7]

The duration of treatment on ART drugs was found to be a determinant covariate in the spiritual domain of the HRQOL of respondents in which extended stay on ART had a positive relationship with spiritual health in the HIV mono-infected patients. This may be because as a patient stays longer on ART, they can learn more about how to manage their health and life.[50] This result is similar with the finding of the study conducted in Addis Ababa, Ethiopia, on HRQOL of HIV mono-infected people on combined ART.[7]

Depressive symptoms were found to be significantly associated with all domains of HRQOL except the level of independence domain of HRQOL in the HIV mono-infected patients. It was also found to be significantly associated with social, environmental, and spiritual domains of HRQOL in HIV/TB co-infected patients. The finding is in parallel with studies conducted in Ethiopia and Nepal[7,16,20] in which depression was significant in all domains.

In this study, stigma was also found to be significantly associated with social, environmental, and spiritual domains of HRQOL in the HIV mono-infected patients; and psychological and environmental domains of the HRQOL in the HIV/TB co-infected patients where participants who were stigmatized had a lower HRQOL on the mentioned domains in both groups compared with non-stigmatized participants. The finding is in line with the findings of different studies conducted in Ethiopia and Nepal.[7,16,17,20]

The study revealed that wealth status had a positive significant association with all the domains of the HRQOL except the spiritual domain in the HIV mono-infected patients. It also had a positive significant association with the physical and psychological domains of the HRQOL in the TB/HIV co-infected patients. This finding is consistent with the findings of the studies conducted in Ethiopia and India.[7,19,21,23]

CD4 count had a positive relationship with the psychological domain of the HRQOL of the HIV mono-infected

patients and WHO clinical stage had a significant relationship with the spiritual domain of the HRQOL in both HIV mono-infected and HIV/TB co-infected patients in which patients with a lower stage (I and II) had a better quality of spiritual health than stage III in the HIV mono-infected patients, and stage III patients had a better quality of spiritual health than stage IV patients in TB/HIV co-infected participants. These findings are comparable with the study conducted in Ethiopia.[22,51]

Strength and Limitations of the Study

This study used six dimensions to measure the health-related quality of life, which makes it more valid than measuring the health-related quality of life by four or fewer dimensions. Besides, comparing the quality of life among HIV mono-infected and TB/HIV co-infected patients gives better information. The other strength of the study was that it used a well-validated and structured instrument for measuring the dependent variables and some independent variables.

The possible limitation of the study was a social desirability bias and a recall bias which might have occurred during interviews, and the presence of possible under- or over-reporting of data, especially regarding wealth status. Besides, variables such as smoking status were categorized as smokers and non-smokers in which daily smokers and occasional smokers were treated as one variable "smokers" while they might not have the same effect on HRQOL of patients.

Conclusion

The HRQOL in TB/HIV co-infected patients was lower in all dimensions of HRQOL compared with HIV mono-infected patients. Education, adherence, depression, and wealth status were the factors significantly associated with all domains of the HRQOL in HIV mono-infected patients whereas education and adherence were factors significantly associated with the physical, social relationships and environmental domains, stigma in psychological and environmental domains, wealth index in the level of independence, social relationships, environmental and spiritual domains, and depression in social relationships and environmental domains were the significant factors in the TB/HIV co-infected study participants. CD4 count was found to be significantly lower in the TB/HIV group than the non-co-infected HIV patients.

Therefore, health-care providers should pay more attention to TB/HIV co-infected patients to improve their quality of life, and management plans should consider interaction with psychiatric centers since depression and stigma were more prevalent. Furthermore, it would be desirable for the government to provide income generation activities and support to improve the wealth status of both the HIV mono-infected and TB/HIV co-infected patients. Finally, further exploration of the factors affecting low HRQOL scores should be conducted using a qualitative method.

Abbreviations

AIDS, Acquired Immunodeficiency Syndrome; AOR, Adjusted odds ratio; ART, Antiretroviral treatment; Cart, Combined antiretroviral treatment; CD4, T-lymphocyte cell bearing CD4 receptor; DOTs, Direct observed treatment/therapy short course; EPTB, Extra Pulmonary Tuberculosis; FAST, Fast Alcohol Screening Test; HAART, Highly active antiretroviral treatment; HIV, Human Immunodeficiency Virus; HRQOL, Health-related quality of life; MDR, Multidrug resistance; PLHIV, People living with Human Immune-deficiency Virus; PTB, Pulmonary Tuberculosis; QOL, Quality of life; SSA, sub-Saharan Africa; TB, Tuberculosis; TB/HIV, Tuberculosis and Human Immunodeficiency Virus; WHO, World Health Organization; WHOQOL-HIV, World Health Organization Quality of Life for HIV; XDR, Extensive drug resistance.

Data Sharing Statement

All the data were included in the study, and data will be available upon a responsible request from the corresponding author.

Ethics Approval and Consent to Participate

Ethical approval was obtained from the Ethical Review Board of the Institute of Public Health, the University of Gondar (Ref. No. IPH/266/2019). Permission letters were obtained from the Amhara Regional Health Bureau and respective hospitals and health centers. After a brief explanation of the purpose, risk, and benefits of the study, written consent was obtained from each participant. All forms and data related to the study were stored in a locked room in a secured area, with controlled access available only to the investigator and supervisors to keep confidentiality. Participation in the study was voluntary, and

individuals were free to withdraw or stop the interview at any time. This study was conducted in accordance with the Declaration of Helsinki.

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Author Contributions

All authors contributed to data analysis, drafting or revising the article, have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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The authors declare that they have no competing interests for this work.

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